

CARDIOGENIC NEUROLOGY

Clinical studies using long-term electrocardiographic
recording

by

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Seek and you will find.

Book of Matthews, chapter 7, verse 7.



To Majvor and Nils-Olof

CONTENTS

Contributing studies	page 4
Introduction	page 6
Aims of the study	page 7
<u>Methods</u>	
Long-term electrocardiographic recording	page 8
Classification of arrhythmias	page 8
Design of contributing studies	page 9
Results	page 12
Discussion	page 27
General conclusions	page 38
References	page 40

This thesis is based upon the following papers referred to within the text by roman numerals:

- I. Abdon, N.-J.: Frequency and distribution of long-term ECG-recorded cardiac arrhythmias in an elderly population with special reference to neurological symptoms. *Acta Med Scand* 209: 175-183, 1981.
- II. Abdon, N.-J., Johansson, B.W. & Lessem, J.: Predictive utility of routine 24-hour electrocardiography in suspected Adams-Stokes' syndrome - Comparison with the cardiac rhythm during symptoms. Submitted for publication.
- III. Abdon, N.-J.: Long-term electrocardiographic recording in suspected Adams-Stokes' syndrome. Part I: Diagnostic aspects. Submitted for publication.
- IV. Abdon, N.-J.: Long-term electrocardiographic recording in suspected Adams-Stokes' syndrome. Part II: Four year follow-up. Submitted for publication.
- V. Abdon, N.-J.: Unrecognized intermittent bradycardias in patients treated for senile dementia. In: *Cardiac Pacing, the Proceedings of the Vth International Symposium*, pp 93-97, Ed. Y Watanabe, Excerpta Medica, Amsterdam, 1977.
- VI. Abdon, N.-J. & Nilsson, B.E.: Episodic cardiac arrhythmia and femoral neck fracture. *Acta Med Scand* 208: 73-76, 1980.
- VII. Abdon, N.-J., Zettervall, O., Berglund, S., Carlson, J., Sterner, G., Tejler, L. & Turesson, I.: Is occult atrial disease a frequent cause of non-hemorrhagic stroke? - Long-term ECG in 86 patients. Submitted for publication.

List of abbreviations

AF	Atrial fibrillation
APA	Atriopathic arrhythmia
APC	Atrial premature contraction
AT	Atrial tachycardia
AVB	Atrioventricular block
AV-bl	
bpm	Beats per minute
BTS	Bradycardia-tachycardia syndrome
LTER	Long-term electrocardiographic recording
SSS	Sick sinus syndrome
TIA	Transient ischemic attack
VPC	Ventricular premature contraction
VT	Ventricular tachycardia

Introduction

For centuries disturbances in cardiac rhythm have been known to cause cerebral ischemic attacks, i.e. the Adams-Stokes' syndrome. Formerly believed to be a rarity, there has been an increased awareness during recent years that the Adams-Stokes' syndrome may in fact be very common. McAllen and Marshall (1) pointed out that such patients present with neurological symptoms and that the underlying cardiac disorder is initially only seldomly suspected. The insidious and episodic character of symptomatic cardiac arrhythmias may well be the main reason why the commonness of the Adams-Stokes' syndrome was not clearly understood until recently. Reflecting the growing recognition of cardiac arrhythmias as a cause of disability and even death, reported incidences for serious bradycardias have continuously climbed during the last two decades. In 1966 Johansson (2) reported an incidence of 63 new cases of atrioventricular block (AVB 3⁰) per million inhabitants and year ($10^6 \text{ inh} \times \text{year}^{-1}$) and recommended wide indications for cardiac pacing. Following the popularization of the sick sinus syndrome (SSS) by Ferrer (3, 4, 5) this disorder is now increasingly being diagnosed. In a recent study of possible pacemaker candidates from the Devon Clinical Area, Shaw and Kekwick (6) observed roughly equal incidences of AVB 2⁰ or 3⁰ and the SSS, respectively, in about 100 new cases per $10^6 \text{ inh} \times \text{year}^{-1}$ during their last sampling years. Lacking further epidemiological studies, pacemaker implantation rates may be used. For 1978 the respective national pacemaker implantation rates were 309 and 181 new implants per $10^6 \text{ inh} \times \text{year}^{-1}$ in the US and Sweden, respectively (7). On the other hand, pacemaker implantation rates reflect only part of the problem. Patients with iatrogenic bradycardias are unlikely to get paced, and tachyarrhythmias are nowadays recognized as a cause of the Adams-Stokes' syndrome (8).

In collaboration with Dr Raoul Malmcrona the author observed in the early 70's that many patients with syncope and/or dizziness had occult previously unknown serious bradycardias when they were subjected to monitoring in a coronary care unit. Frequently these patients had a history of accidents, and despite previous work-up many of them were earlier diagnosed as suffering from cerebral atherosclerosis, epilepsy or even dementia. A concept of "cardiogenic neurology", i.e. the active diagnosis and treatment of arrhythmias in symptomatic patients, was adopted, and increased facilities for the diagnosis of episodic arrhythmias were arranged. This resulted in a dramatic increase of the local pacemaker implantation rate (9).

The present study is a summary of contributions to the field of "cardiogenic neurology". The objective has been to compile an increased clinical understanding of the role of episodic cardiac arrhythmias in various cerebral

manifestations and disability patterns.

Specific aims and general design

The approach to the main objective was separated into the following steps:

1) Which arrhythmias are significant?

Arrhythmias known or presumed to cause cerebral symptoms were termed significant. With the purpose of establishing valid and strict criteria for significant arrhythmias applicable to the age groups of clinical concern, an elderly population was selected at random and subjected to 24-hour long-term electrocardiographic recording (LTER) (I). Arrhythmias associated with complaints of syncope and dizziness in this population were regarded as significant.

The adequacy of the classification of significant arrhythmias according to (I) was then tested in patients with suspected Adams-Stokes' syndrome by prolongation of LTER until symptoms had occurred (II).

2) Which significant arrhythmias are detectable among patients with suspected Adams-Stokes' syndrome and other possible manifestations of episodic arrhythmic cerebral ischemia?

The prevalence of episodic and significant arrhythmias was investigated in different patient categories: Suspected Adams-Stokes' syndrome (III), dementia (V), or fracture of the femoral neck (VI).

3) What is the effectiveness of therapy for significant arrhythmias?

In a series of 173 patients with suspected Adams-Stokes' syndrome and significant arrhythmia, a 3 to 5 year follow-up was conducted. The results of therapy on symptoms of syncope and/or dizziness and the long-term need for permanent geriatric hospitalization were analysed with respect to types of significant arrhythmia (IV).

4) May certain types of significant arrhythmias be associated with cerebrovascular manifestations other than general ischemic attacks?

In a consecutive series of patients with non-hemorrhagic stroke, the prevalence of significant occult atrial arrhythmias known to be associated with cerebral embolizations was investigated (VII).

Methods

LTER

LTER was performed using portable one-channel ECG-recorders type SRA/HRB-2 or SRA/HRB-3 (Helcomed Norden/Hellige). The screening of ECG-tapes has been detailed in paper I. Briefly, all ECG-tapes were screened by either of two automatic units both producing an ECG write-out when an arrhythmia was detected. One unit was set to produce write-outs for rates ≥ 120 and ≤ 40 beats per minute (bpm), as detected by single R-R-interval analysis, whereas the other unit produced a write-out when the rate differed up- or downward by 30% or more compared to the average of the last minute of recording. In addition, both units produced write-outs for every 10th ventricular premature contraction (VPC) as detected by QRS-configuration criteria and occurring within one minute.

All write-outs were initially scrutinized by specialized laboratory technicians and finally by the author. Technically doubtful or missing recordings were always repeated until a satisfactory result was obtained.

Classification of arrhythmias

The highest occurring frequency of observed ectopic beats was recorded according to the following criteria: Infrequent = one ectopic per more than 10 beats, moderately frequent = one ectopic per 6-10 beats, and frequent = one ectopic per 5 or less beats. A sequence containing three or more ectopic beats was used in the grading of ectopic intensity. Potentially dangerous VPCs according to Lown and Wolf (10) were recorded.

Heart rates were measured from a sequence of three or more beats. A tachycardia - whether ventricular or atrial - consisted of three or more consecutive beats. Ventricular tachycardia (VT) had a rate of 100 bpm or more and atrial tachyarrhythmias a rate of 120 bpm or more. No attempts were made to separate atrial and nodal tachycardias. Atrial fibrillation and flutter (AF), however, were recorded separately. Nodal tachycardias were referred to atrial tachycardias (AT).

In persistent atrial fibrillation AVB 3⁰ was considered present when the heart rate was 40 bpm or less or occasionally 41-50 bpm, when there was an evident escape rhythm.

The sick sinus syndrome fulfilled one or more of the following criteria as derived from paper I: 1) Sinus brady-arrhythmia ≤ 50 bpm with a variation of $\geq 20\%$ in consecutive P-P-intervals, 2) Regular sinus bradycardia ≤ 45 bpm when awake, 3) Sino-atrial block or 4) Sinus arrests of ≥ 1.5 sec. Patients with additional episodes of AF or AT were considered to have the bradycardia-tachycardia syndrome (BTS) variety of the SSS. All individuals with the SSS were referred to this group irrespective of any additional arrhythmias.

All patients with AVB 2^o or 3^o were referred to this group provided no concomitant signs of the SSS were detected. All patients with ventricular arrhythmias were referred to this group provided no signs of bradycardia were present. Patients with atrial tachy-arrhythmias were listed separately provided they had no other concomitant significant arrhythmias.

Statistical analysis

The chi-square test including Yates' correction was applied unless otherwise stated.

Design of contributing investigations

Paper I: Significant arrhythmias in an elderly population selected at random. For each patient collected within the first year of sampling for papers III and IV an age-and-sex-matched individual was selected at random by the Population Actuary in Malmö. This resulted in the invitation of 157 individuals aged 47-92 years (mean $\pm$ SD 71 $\pm$ 11) to participate in the study.

Actively participating individuals (103) were subjected to a careful physical examination and a laboratory profile was made. Symptoms of dizziness and/or syncope during the last two years were recorded. All individuals were then examined by approximately 24 hours of applied LTER.

Individuals not participating actively (54) were evaluated separately.

By comparing the arrhythmias detectable among individuals with and without syncope and/or dizzy spells criteria of significant arrhythmias were established.

Paper II: Predictive utility of routine 24-hour electrocardiography in suspected Adams-Stokes' syndrome - comparison with the cardiac rhythm during symptoms.

The adequacy of the criteria of significant arrhythmias as derived from (I) was tested in 81 patients who had consented to wear the ECG tape recorders until the cardiac rhythm could be recorded during symptoms and who were willing to keep diaries. The suggestion of the Adams-Stokes' syndrome being or not being the cause of symptoms as judged from the initial 24-hour recording was compared with the cardiac rhythm during symptoms. The predictive utility of significant arrhythmias as defined by (I) was then evaluated.

When symptoms failed to develop, the initial 24-hour recording was

compared with an additional 24-hour recording for the evaluation of the increased yield of significant arrhythmias obtainable by prolongation of LTER from 24 to 48 hours.

Paper III: Long-term electrocardiography in suspected Adams-Stokes' syndrome.

Part I: Diagnostic aspects.

Three hundred and thirty consecutive patients with suspected Adams-Stokes' syndrome were investigated. These patients were investigated while hospitalized in the Medical Department or seen as out-patients by the author.

The frequency of distribution of significant arrhythmias was analysed utilizing the classification of significant arrhythmias from (I).

The absence or presence of episodic and significant arrhythmias was related to patient ages and cardiac and neurological complaints versus objective findings. The fractions of patients with various settings of symptoms having significant arrhythmias were assessed. Attempts were made to determine among patients with clinically suspected Adams-Stokes' syndrome, which are most likely to have significant arrhythmias.

Paper IV: Long-term electrocardiography in suspected Adams-Stokes' syndrome.

Part II: Four year follow-up of patients with significant arrhythmia.

Among the 330 patients of (III) 173 had significant arrhythmias. A 3 to 5 year follow-up was conducted; no patient was lost in this follow-up study.

The results of therapy for significant arrhythmias as regards symptoms of syncope and/or dizzy spells was evaluated in terms of improvement of persisting symptoms. Comparisons were made with patients not subjected to therapy.

The possible long-term prevention of need of permanent geriatric hospitalization was evaluated with respect to type of arrhythmia and therapeutic intensity. The role of arrhythmias associated with cerebral embolizations was evaluated. Finally, the place and mode of death were analysed in order to determine whether death in patients with significant episodic arrhythmias was associated with a sudden or short-term illness or followed a long-standing downhill course.

Paper V: Unrecognized intermittent bradycardias in patients treated for senile dementia.

All patients from two wards treating demented patients in a psychogeriatric hospital were subjected to 24-hours of applied LTER.

The 49 patients who had acceptable recordings were divided into two groups. One consisted of 17 patients with end-stage psychiatric disorders designated as terminal dementia, the other consisted of 32 patients with a designation of "atherosclerotic" or postapoplectic dementia in a broad sense.

The significant arrhythmias detected were related to previous possible manifestations of general ischemic cerebral attacks such as fractures and diagnosed epilepsy.

Due to the findings made among these hospitalized and demented patients, another group of demented patients was later added. These patients were generally free from somatic disabilities but completely disorientated and therefore in nursing home care.

Paper VI: Episodic cardiac arrhythmia and femoral neck fracture.

Fifty-eight consecutive patients with recent fracture of the femoral neck were investigated by 24 hours of applied LTER using the classification of significant arrhythmias as derived from (I). The fraction of patients having significant arrhythmias was assessed.

Patients with and without significant arrhythmias were evaluated with respect to cerebral symptoms suggesting significant arrhythmias prior to the fracture in order to evaluate whether the arrhythmias may have caused the fall leading to fracture. Finally, the short-term prognostic implications of significant arrhythmias in patients with fracture of the femoral neck were evaluated.

Paper VII: Is occult atrial disease a frequent cause of non-hemorrhagic stroke?
- Long-term ECG in 86 patients.

In order to assess the importance of occult atrial disease and arrhythmia with possible embolization as a cause of non-hemorrhagic stroke, 86 consecutive patients were investigated by approximately 24 hours of applied LTER.

A concept of occult atrio-pathic arrhythmias was developed and tested and the use of LTER as a mean of diagnosing them was evaluated

Results

Paper I: Insignificant arrhythmias in asymptomatic elderly individuals.

Seventy-seven of the 103 active participants in this study had not experienced syncope and/or dizzy spells during the last two years prior to the study. The normally occurring and insignificant arrhythmias as detectable by LTER were determined among this group.

Table I. Insignificant arrhythmias in 77 elderly asymptomatic individuals.

Arrhythmia	n	%
APCs		
Infrequent	42	55
Moderately frequent or frequent	15	19
Atrial tachy-arrhythmias		
120 bpm $\leq$ 8 sec	7	9
VPCs		
Infrequent	21	27
Moderately frequent or frequent	6	8
Regular sinus bradycardia during night sleep	20	26

Table I summarizes the insignificant arrhythmias detected among asymptomatic elderly individuals. Only 4 had no arrhythmia at all while monitored. Although 42 of the 57 having APCs and 21 of the 27 having VPCs had only infrequent or moderately frequent ectopic beats, a considerable fraction of 19% and 8%, respectively, had frequent or moderately frequent APCs or VPCs. Short bursts of atrial tachy-arrhythmias - usually lasting only some few seconds but occasionally lasting up to 8 seconds - were noted among 7 (9%). Remarkably common was the occurrence of sinus bradycardia 41-50 bpm at the time of night sleep - 20 (26%). Typical for this sinus bradycardia during night sleep was the perfectly regular pattern as compared to patients with the SSS who almost always had episodes of sinus arrhythmia when bradycardic.

Significant arrhythmias in symptomatic versus asymptomatic patients (Table II)

Table II. Significant arrhythmias in symptomatic versus asymptomatic individuals.

Arrhythmia	Symptomatic n = 26	Asymptomatic n = 77	p
Atrial tachyarrhythmia ≥ 120 bpm ≤ 8 sec	1	2	N.S.
Frequent VPC with R-on-T-types	2	0	N.S.
SSS	6	3	< 0.02
AVB 2 ⁰ or 3 ⁰	<u>3</u>	<u>0</u>	< 0.05
	12	5	< 0.001

Twenty-six of the 103 active participants had experienced dizzy spells or syncope during the last two years prior to the study. This figure includes one who was paced due to the SSS and one who was paced due to AVB 3⁰, as they appeared. Both had cerebral symptoms prior to the pacemaker implantations.

Significant arrhythmias occurring predominantly among symptomatic patients are summarized in Table II. Twelve (46%) had significant arrhythmias as compared to 5 (6%) of the asymptomatic individuals ($p < 0.001$). If also frequent VPCs without R-on-T-types are to be considered significant a total of 9 of the 77 asymptomatic individuals had significant arrhythmia. Frequent VPCs with R-on-T forms and AVB 2⁰ or 3⁰ were detected exclusively in symptomatic patients while 2 of 3 instances of atrial tachyarrhythmias > 8 sec and 3 of 9 instances of the SSS occurred among asymptomatic subjects. The 3 cases of the SSS detected among asymptomatic individuals had definite signs of sino-atrial dysfunction: two had bradycardias of 34 and 36 bpm, respectively, and the third had long-standing episodes of sino-atrial block without bradycardia. Furthermore, the widening of the criteria applied for the SSS to include cases with sinus bradyarrhythmia ≤ 55 bpm or sinus bradycardia ≤ 50 bpm when awake would not have caused the inclusion of more subjects into the group of cases with the SSS.

The classification of frequent VPCs and atrial tachyarrhythmias > 8 sec as significant in symptomatic subjects, despite their occurrence in asymptomatic individuals, will be discussed later.

Analysis of subjects not actively participating

The 54 (34%) drop-outs may have influenced the general trend of findings in the study. This was analysed by a separate study.

Forty-nine of the 54 drop-outs could be properly assessed by a perusal of recent records from the departments of the General Hospital in Malmö in 38 and by personal interviews in the remaining 11. Thirty-one had ECGs stored in the General Hospital, 29 of them being no older than 2 years.

The percentages of subjects with syncope and/or dizzy spells were similar among active participants and drop-outs, 25% and 32%, respectively. Arrhythmias of all kinds were detectable in the resting ECGs (or previously monitored ECGs, if performed) of 10 (20%) of the 49 traced drop-outs as compared with 13 (13%) of the actively studied subjects (N.S.).

Need for treatment of cardiac arrhythmias

Although not being the intended purpose of the study, the discovered need for treatment of arrhythmias may be of interest. Eleven patients, ten of them having symptoms, had indications for treatment: 4 received treatment for tachyarrhythmias, 4 had drugs omitted for iatrogenic bradycardias and 3 were offered cardiac pacemakers, the latter in addition to the 2 already paced before the study. The indications for cardiac pacing were in accordance with those accepted by an international expert panel (11): AVB 3⁰ or symptomatic SSS with bradycardia ≤ 40 bpm.

Paper II: Predictive utility of routine 24-hour electrocardiography in suspected Adams-Stokes' syndrome - comparison with the cardiac rhythm during symptoms.
Eighty-one patients with suspected Adams-Stokes' syndrome with frequent attacks were included. In 43 patients the cardiac rhythm was recorded during symptoms. Thirty-eight patients, however, were later unable to accept the continuation of ECG recording until symptoms had developed.

Patients with the cardiac rhythm recorded during symptoms

Table III is a summary of findings in patients monitored until symptoms occurred. Twenty-two patients had no significant arrhythmia during the asymptomatic 24-hour recording, two of them having AF/AT

while monitored until symptoms occurred, but in 20 the absence of significant arrhythmia during symptoms was confirmed.

Table III. Patients examined by LTER until appearance of symptoms. Comparison of 24-hour recording with and without symptoms occurring. Arrows indicate cases with a new arrhythmia diagnosis after prolongation.

Arrhythmia	Patients with arrhythmias present during 24-hour period		Patients with normal rhythm during symptoms
	without symptoms	difference	with symptoms
No significant	22	- 2 ↓	20
Atrial tachyarrhythmias	7	+ 2 - 1	8
Sick sinus syndrome		↓	
Brady-tachy	6	+ 1	7
Bradycardia only	1	± 0	1
Atrioventricular block 3 ^o	1	± 0	1
Frequent VPCs	2	± 0	2
VPC-couplets/Ventricular tachycardia	4	± 0	4

A total of 23 patients had significant arrhythmia, the presence of significant arrhythmias being observed during the asymptomatic recording in 21 of them. However, one patient with AF initially and during symptoms had episodes of sinus bradycardia without relationship to symptoms allowing a correct diagnosis of the BTS by prolonged recording. Thus, freedom from significant arrhythmias during an asymptomatic 24-hour period resulted in the recording of a normal cardiac rhythm during symptoms in 90% of the cases. The probability of finding a previously undiagnosed significant arrhythmia or a new type of significant arrhythmia, if the initial recording was negative was 13%. On the other hand, only 17 of 23 patients with significant arrhythmias had a temporal relationship between arrhythmia and symptoms. The prediction that a significant arrhythmia detected during an asymptomatic 24-hour recording would be clearly related to symptoms was 73% (15 of 21). By recording an essentially normal rhythm during symptoms, it was initially believed that 6 of the 23 cases with significant arrhythmia could be ruled out from having the Adams-

Stokes' syndrome. This view could not be maintained as in 4 of the 6 initially ruled out, their symptoms disappeared after 1 had been paced and three had been given antiarrhythmic medications. Hence the predictability of definite later evidence relating the arrhythmia to symptoms was 73% but in total of 91% the information of significant arrhythmias being detected was clinically useful.

In 15 of the 17 patients recorded with findings of a significant arrhythmia simultaneous with symptoms, the arrhythmia was not remarkably more advanced than observed at other occasions without concomitant symptoms. Remarkable aggravations were noted only in two patients: one with AVB 3⁰ had an asystole of 21 sec and one with VPC couplets had a long-standing VT when they fainted.

Patients without symptoms

(Table IV)

Table IV. Patients without symptoms during monitoring. Comparison of significant arrhythmias present during a 24-hour initial period and diagnosis after a second 24-hour period. The arrow indicates a patient with a new arrhythmia diagnosis after prolongation.

Arrhythmia	Patients with arrhythmias during 24-hour period		with 2nd period included	Patients with new additional type of significant arrhythmia
	initially	difference		
No significant arrhythmia	19	- 1	18	
Atrial tachyarrhythmias ≥ 120 bpm > 8 sec	5	$\downarrow$ + 1	6	1 (VPCs)
Sick sinus syndrome				
brady-tachy	4	0	4	1 (VPCs)
brady	4	0	4	
AV-dissociation	1	0	1	
Atrioventricular block 2 ⁰ /3 ⁰	3	0	3	1 (VPCs)
Frequent VPCs	1	0	1	
VPC-couplets	1	0	1	

Table IV summarizes the findings in 38 patients who, despite efforts, failed to develop symptoms. Among these, the routine 24-hour recording was compared with the total yield of significant arrhythmias obtained by prolongation of LTER to 48 hours.

Nineteen patients had no significant arrhythmia during the initial 24 hours of LTER. After prolongation of LTER to 48 hours, 18 were still without significant arrhythmia while one had a significant arrhythmia. Again, this was a case of atrial tachyarrhythmia. Thus, 19 of the 20 patients with significant arrhythmias were detected within 24 hours of LTER. However, in 3 prolongation revealed additional significant ventricular arrhythmia. Thus a negative 24-hour recording had a predictability of 95% that a second monitoring period would remain negative. Furthermore, the prediction that patients with significant arrhythmias as detected during a routine LTER of 24 hours would have no new types of significant arrhythmias was 84%.

Common trends in both groups

It was noteworthy that 15 out of the 16 cases with the SSS and all 4 with AVB 2⁰/3⁰ were detected within the first 24 hours. Prolonged monitoring revealed predominantly tachy-arrhythmias: 3 of 14 patients with AF/AT and significant ventricular arrhythmia in 3 patients otherwise considered to have other types of arrhythmias only.

Paper III: Long-term electrocardiographic recording in suspected Adams-Stokes' syndrome. Part I: Diagnostic aspects.

Main arrhythmia diagnosis

Table V. Main arrhythmia diagnosis in 330 patients and in 77 asymptomatic elderly individuals.

Arrhythmia	In suspected Adams-Stokes' syndrome n = 330		In asymptomatic elderly individuals n = 77		P
	n	%	n	%	
No significant	157	48	68	88	<0.001
SSS	68	21	3	4	<0.001
AVB 2 ⁰ or 3 ⁰	29	9	0	0	<0.02
AF/AT $\geq$ 120 bpm $>$ 8 sec	29	9	2	3	N.S.
Frequent VPCs	15	5	4	5	N.S.
VPC couplets/VT	32	10	0	0	<0.02

The number of patients referred to the various groups of main arrhythmia diagnosis are given in Table V. The corresponding numbers of elderly asymptomatic individuals having the respective arrhythmia

are given for comparison. As frequent VPCs also without potentially dangerous forms may be regarded as significant arrhythmias in symptomatic patients and as insignificant arrhythmias in asymptomatic patients, they are also given for comparison. The reasons for this view regarding VPCs will be discussed later.

In 173 (52%) of the 330 patients significant arrhythmias were detected. Among the 68 cases of the SSS 32 were purely bradycardic, while 36 had the BTS. AVB 2⁰ or 3⁰ was found in 29 patients, 5 having 2⁰ and 24 3⁰ AVB.

Significant arrhythmias in relation to age

In patients not older than 39 years, 18% had significant arrhythmias. The fraction of patients having significant arrhythmias then climbed with age and reached 78% for patients aged 80 years or more. This increase with age is significant (contingency table test, $p < 0.001$).

Neurological symptoms in relation to significant arrhythmias

Syncope and dizzy spells: Among 117 patients with 2 or more syncopes and dizzy spells, 70 had significant arrhythmias and 47 had not. In 37 patients who had experienced 2 or more syncopal episodes but had no dizzy spells, only 12 had significant arrhythmias. This increase in the fraction of patients with significant arrhythmias among those suffering from both syncopes and dizziness, as compared with those having only syncopes, was significant ($p < 0.001$). A single syncope was experienced by 24 patients having, and 17 not having significant arrhythmia, 19 of the former and 11 of the latter had had additional dizzy spells. Dizzy spells without syncope was experienced by 135 patients, 67 with, and 68 without significant arrhythmias.

Miscellaneous : 70 of the patients had previously been classified as having cerebral atherosclerosis which did not affect the probability of finding significant arrhythmias. Cerebrovascular accidents with focal neurological symptoms were experienced by 74 patients and equally distributed in patients with and without significant arrhythmias. Thirty of the 157 patients without, but also 23 of the 173 patients with significant arrhythmias stated that their symptoms occurred only in the up-right position or when rising up. Previous treatment for hypotension was equally common in both groups, 12 of 153 without, and 14 of 173 with significant arrhythmias. Paroxysmal fatigue was an outright complaint made by 41 of the 173 and 14 of the 157 patients with and without significant arrhythmias,

respectively ($p < 0.001$).

Cardiac symptoms in relation to significant arrhythmias

Subjectively experienced arrhythmias: Thirty-six of the 157 patients without and 57 of the 173 with significant arrhythmias had experienced a "fast" cardiac action ($p < 0.05$). Among the 57 patients with significant arrhythmias and subjective tachycardias, however, 31 had a main arrhythmia diagnosis of bradycardia. An "irregular" cardiac action was experienced by 9 of the 157 patients without and by 22 of the 173 patients with significant arrhythmias ($p < 0.05$). A "slow" pulse was noted by 31 patients (or their relatives) with, but also by 9 patients without significant arrhythmias ($p < 0.001$). Nine patients with tachy-arrhythmia had experienced a "slow" pulse.

Angina etc.: Angina at effort was equally common in patients with and without significant arrhythmia, 13 and 10, respectively. Angina at rest or other types of chest pain was a more common symptom in patients with than without significant arrhythmia, 50 and 32 patients, respectively (N.S.).

Objective cardiac findings in relation to significant arrhythmias

According to the case records, 25 patients had had an earlier interpretation of digitalis intoxication with arrhythmias that disappeared when the drug was withheld: 17 had had bradycardias, 6 had had VPCs and in 2 the exact nature of arrhythmia was never documented by ECG. Twenty-two of these 25 patients were found to have significant arrhythmias but 3 had not ($p < 0.001$).

Twenty-four of the 157 patients without, and 65 of the 173 with significant arrhythmias received digitalis or diuretics for heart failure, a significant difference ($p < 0.001$). In particular patients with the finding of bradycardias were prone to have treatment for heart failure. Radiological heart enlargement was noted in 21 of the 157 patients without and by 73 of the 173 patients with significant arrhythmia. Previous myocardial infarctions - definite or suspected - had occurred in 15 of 157 patients without and in 29 of 173 patients with significant arrhythmias, respectively (N.S.). Valvular disease was equally found in patients with and without significant arrhythmia, 5 and 4 cases, respectively.

The routine ECGs showed sinus rhythm in 301 patients and permanent AF in 29 patients, 5 without and 24 with significant arrhythmia

($p < 0.001$). Bradycardias ≤ 55 bpm or an R-R-interval of ≥ 1.5 sec were present in 46 patients, 40 of whom had significant arrhythmia during LTER ($p < 0.001$). Bundle branch blocks, however, were about as common in patients with as in patients without significant arrhythmias, 30 of 173 and 23 of 157 patients, respectively. Bifascicular block was equally common in both categories of patients, 4 and 3 cases, respectively. Interestingly, 10 of 30 patients with significant arrhythmia and bundle branch block had tachy-arrhythmia during LTER.

APCs were found in the standard ECG of 8 of 157 patients without and 25 of the 173 patients with significant arrhythmia ($p < 0.02$). VPCs were observed in the routine ECGs of 34 of 173 patients with and 9 of 157 patients without significant arrhythmia ($p < 0.001$).

Paper IV: Long-term electrocardiographic recording in suspected Adams-Stokes' syndrome: Part II: Four year follow-up.

The 173 patients with significant arrhythmias described in paper III were subjected to a 3-5 year follow-up. Therapy for arrhythmia was given as considered indicated by the physician in charge of the patient.

Symptoms of syncope and/or dizziness in relation to therapy

Effectiveness of therapy for bradycardias

Digitalis omitted/reduced (and not later paced): In 20 patients with bradycardias digitalis was reduced (5) or omitted (15). LTER was repeated in 14, all having virtually no remaining bradycardias. Among these 20 patients, 16 responded to therapy with complete or almost complete freedom from symptoms.

Atropine or sympathicomimetics: Two patients with the SSS received atropine but only one of them improved. Four patients with the SSS and one with AVB 3⁰ were given sympathicomimetics, all with improvement of symptoms.

Pacing: Including 4 patients who previously had had their digitalis omitted 27 patients were paced. Twenty-three of these had definitely reduced syncope and/or dizziness, but in four symptoms persisted.

Miscellaneous: Six patients with mainly tachy-arrhythmic SSS were given antiarrhythmic treatment which resulted in complete or almost complete relief from symptoms in four of them. In 3 patients, beta-

blockers triggering bradycardias in the SSS were omitted, 2 of them improving. One patient with mild bradycardia in the SSS achieved freedom from cerebral symptoms as he was treated for a concomitant hypotension, and one patient with a hypokalemia returned to normal cardiac rhythm following proper substitution therapy.

Not paced despite recommendation: Nine patients were not paced despite recommendation by a cardiologist. Two of them died before evaluation of any persisting symptoms could be performed. Six of the remaining 7 patients had persisting symptoms of syncope and/or dizziness but one improved spontaneously.

No treatment: Twenty patients received no treatment for bradycardias including 4 patients in whom continuation of digitalis medication was considered essential for heart failure. Seven of them improved as regards symptoms of syncope and/or dizziness but in 13 symptoms persisted.

Digitalized: In three patients the bradycardias were obviously disregarded and the patients later digitalized due to heart failure. They all then deteriorated.

Summary of the results of therapy for bradycardia

In the 65 patients who were subjected to active and adequate therapy, 53 experienced complete or almost complete freedom from cerebral symptoms during the follow-up averaging four years. Among the 30 who had inadequate or no therapy at all, only 8 (27) improved, while 22 had persistent symptoms.

Effectiveness of therapy for AF/AT

Digitalis: Digitalis-induced AF/AT was diagnosed in 5 patients. When the drug was withdrawn, all experienced improvement of cerebral symptoms. It was commenced in 7 patients previously not digitalized, 6 of them responding well.

Other therapies: Four patients were given antiarrhythmic drugs, all reporting freedom from cerebral symptoms. Eight patients received betablockers for AF/AT, 6 experiencing improvement of symptoms.

No therapy: Five patients received no active treatment for AF/AT. One recovered spontaneously, but 4 continued to have troublesome symptoms.

Effectiveness of therapy for frequent VPCs

Digitalis: Withdrawal of digitalis was successfully performed in 3 patients with improvement of symptoms.

Other therapies: Seven patients received anti-arrhythmics which were effective in 6. Two patients with alcohol consumption had improvement of both arrhythmia and symptoms following a reduction of their alcohol intake.

No therapy: No active treatment was given in 3 cases and these continued to have symptoms.

Effectiveness of therapy in VPC couplets/VT

Digitalis: Two patients were improved when digitalis was withdrawn.

Other therapies: Twenty-two patients, including three in whom digitalis withdrawal was initially performed without success, were treated with anti-arrhythmics. After the initial treatment with a single drug or digitalis withdrawal LTER was repeated in 17. The simultaneous use of two or more anti-arrhythmic preparation was then needed in 4 or them to achieve freedom from malignant ventricular arrhythmias and relief from symptoms. Twenty-one of these patients improved.

One patient was effectively treated for his ventricular arrhythmia by withdrawal of levodopa but his cerebral symptoms persisted. One patient observed that his symptoms disappeared when he discontinued use of a terbutaline inhalation spray for bronchial asthma.

No therapy: Six patients who were not given therapy continued to have symptoms.

Summary of the effectiveness of therapy for tachy-arrhythmias

Sixty-two patients received anti-arrhythmic treatment considered to be adequate, 56 of them responding well but 6 continuing to have cerebral symptoms. In contrast, only one out of 14 patients not treated reported complete or almost complete freedom from cerebral symptoms.

Long-term geriatric hospitalization

During follow-up, 35 patients were admitted to permanent geriatric hospitalization. Patients with bradycardia had a greater subsequent need of permanent geriatric hospitalization than patients with tachy-

arrhythmias, 24 out of 97 and 11 out of 76, respectively (N.S.). Among patients treated by pacing or digitalis withdrawal /reduction for bradycardias 15 of 47 needed permanent geriatric hospitalization as compared to 9 of 50 less actively or not treated (N.S.).

A total of 126 patients had atriopathic arrhythmias defined as permanent AF, a main arrhythmia diagnosis of atrial arrhythmia or significant atrial arrhythmia in addition to other main arrhythmia diagnoses. Among the 126 patients with atriopathic arrhythmias 31 were later admitted to permanent geriatric hospitalization as compared to 4 of 47 patients without atriopathic arrhythmias ($p < 0.05$).

Deaths and autopsy findings

Seventy patients died during follow-up. Six died a sudden possibly arrhythmic death, 2 of them being not paced despite recommendation and 3 with the SSS following digitalization. Twenty-eight died while in permanent geriatric care indicating a long-standing downhill course, while 36 died following short-term illness.

Forty-five of the 63 patients subjected to autopsy had either severe coronary atherosclerosis or myocardial scars of all ages. Encephalomalacias were found in 28 patients, 11 of whom had no or only minimal cerebral atherosclerosis. Five patients died from possible non-cerebral embolization and 16 further patients had possible splenic or renal infarctions.

Paper V: Unrecognized intermittent bradycardias in patients treated for senile dementia.

All 63 patients in two wards treating exclusively demented patients in a psychogeriatric hospital were studied. Acceptable recordings were obtained in 49 patients.

At the time of this study the criteria for significant arrhythmias were not developed and the patients were classified empirically with respect to what was then considered to be serious arrhythmias. The differences in comparison with the other studies are: VPCs were considered frequent only when a bigeminy or trigeminy was present and the duration requirement of AF/AT was not applied.

Table VI. Serious episodic arrhythmias in relation to type of dementia.

Arrhythmia	Type of dementia		Total n = 49
	Postapoplectic n = 32	"Terminal" n = 17	
SSS	3	2	5
AF/AT	6	3	9
AVB 2 ⁰ /3 ⁰	8	0	8
Ventricular bigeminy, trigeminy, VT	3	1	3

Table VI summarizes the serious arrhythmias detected. Twenty (63%) of the 32 patients with postapoplectic dementia and 6 (35%) of the 17 patients with terminal dementia had serious arrhythmias. The difference between the groups is not significant.

Arrhythmias in relation to previous fractures

Twenty-three patients had no serious arrhythmia while 26 had. Six and 16, respectively, had suffered from previous fractures ($p < 0.05$). Thirteen of them had suffered from fracture of the femoral neck.

Arrhythmias in relation to neurological symptoms

Nineteen patients were previously hospitalized due to epilepsy (5) or "cerebrovascular accidents" without focal neurological signs (14). Five of them were among the 23 without, and 14 among the 26 patients with serious arrhythmias ($p < 0.05$).

Survival

The patients were followed for 30 months. Eight patients without, and 16 patients with serious arrhythmias died. The average time between admission and death for patients with serious arrhythmias was 4 years.

Paper VI: Cardiac arrhythmia and femoral neck fracture.

Fifty-eight consecutive patients with recent fracture of the femoral neck were studied by LTER.

Significant arrhythmias

Thirty-five patients had no significant arrhythmia while 23 (40%) had. The SSS was found in 2, AF/AT in 9, frequent VPCs in 9, and AVB 2^o or 3^o in 3 patients, respectively.

Mortality and discharge in relation to significant arrhythmia

Five of the 23 patients with, and 4 of the 35 without significant arrhythmia expired during hospitalization. This increased mortality rate, however, was not statistically significant.

Despite uncomplicated fracture healing, only 4 of the 18 surviving patients with significant arrhythmias could return to their own homes after discharge due to impaired general condition as compared with 15 of the 31 survivors without significant arrhythmias, again a non-significant difference. On the other hand, only 4 of 23 patients with significant arrhythmias survived and returned home as compared with 15 of the 35 without significant arrhythmia ($p < 0.05$).

Previous dizziness and significant arrhythmia

Fifteen of the 23 patients with, and 12 of the 35 patients without significant arrhythmias had visited the Medical Department because of syncope and/or dizziness or admitted this type of symptoms prior to the fracture ($p < 0.05$).

Paper VII: Occult atrial arrhythmia in non-hemorrhagic stroke.

In this study 86 patients were studied by means of 24 hours of LTER. Patients with atrial arrhythmias known to, or presumed to cause systemic embolization were termed atriopathic. Such atriopathic arrhythmias (APA) were the SSS, permanent AF and episodic AF/AT irrespective of durations.

Atriopathic arrhythmias in relation to type of stroke (Table VII)

Table VII. Atriopathic arrhythmias in relation to type of non-hemorrhagic stroke and among unselected normal elderly individuals.

Type of stroke	n	AF/AT	SSS	Total with APA	
				n	%
TIA	18	4	2	6	33
Cerebral thrombosis	33	7	8	15	45
Cerebral embolization	35	6	11	17	49
Normal population	103	14	9	23	22

Table VII gives the number of patients with APA in relation to clinical type of stroke and among the normal population. The total figure of 38/86 cases of non-hemorrhagic strokes having atriopathic arrhythmias as opposed to 22/103 normal elderly individuals differs significant ($p < 0.025$). Fifteen of the 21 cases with the SSS had the BTS-type.

Comparison with the standard admission ECG

The standard admission ECG showed atriopathic arrhythmia in 17 (20%) as compared with the 38 (44%) having it during LTER.

Previous stroke and APA

Of the 68 patients with cerebral embolization or thrombosis 52 had no previous strokes in other vascular regions while 16 had. Nineteen of the former and 13 of the latter had APAs. This increased prevalence of APAs among patients with multifocal strokes is significant ($p < 0.05$).

Evidence of prior APA

Eight of the 21 patients with the SSS and 7 of the 17 patients with AF/AT had ECG-documentation of APA prior to the stroke.

Non-cerebral systemic embolizations

Four of the 38 patients with APAs had previously suffered from non-cerebral arterial embolizations. One of the 48 patients without APA had experienced a non-cerebral arterial embolization, and this was

in connection with an acute myocardial infarction (N.S.).

Hypertension. Previous myocardial infarctions

Patients with treatment for hypertension according to their records or with a systolic blood pressure ≥ 175 or diastolic ≥ 115 mm og Hg on admission were classified as hypertensive. Seventeen of 35 hypertensive patients and 21 of the 51 non-hypertensive patients had APA. Nine out of 20 patients with, and 29 of 66 patients without previous myocardial infarctions had APAs. Neither difference was significant.

Aorto-cervical angiograms and APAs

Aorto-cervical angiograms were performed in patients with TIA or when a first TIA could not be excluded, and who were considered for possible carotid surgery. In 20 patients with appropriately located vascular lesions only 3 had APAs, while 3 of 6 patients without such lesions had APAs.

Discussion

What arrhythmias are significant? - Possible solutions

Some doubt exists as to what arrhythmias are significant, i.e. linked with cerebral symptoms. Some light may be thrown on this problem in a number of ways. This study used 3 methods:

- 1) Arrhythmias present in healthy individuals of ages corresponding to those of clinical concern may be compared with the arrhythmias present in symptomatic individuals (Paper I, disc p 27),
- 2) The predictive utility of a classification of significant arrhythmias may be tested by recording the cardiac rhythm during symptoms (Paper II, disc p 24)
- 3) The response to treatment of these arrhythmias may be assessed (Paper IV, disc p 36).

Arrhythmias in unselected elderly subjects (Paper I)

A group of 157 elderly individuals was selected at random and 103 of them actively participated in LTER for approximately 24 hours. This design permitted the establishment of a distinction as clear as possible between significant and insignificant arrhythmias.

No less than 74% of asymptomatic elderly subjects had APCs of various intensities during LTER. APCs found during LTER therefore is an insignificant arrhythmia. AF/AT for 8 sec or less occurred in 9% of asymptomatic individuals. Episo-

des lasting for more than 8 sec were equally common in symptomatic and asymptomatic individuals. However, two reports indicated that some patients do not tolerate AF/AT. Walter et al (12) reported temporal relationships between atrial tachy-arrhythmias and cerebral symptoms and Goldreyer et al (13) demonstrated dramatic hemodynamic consequences of AT in middle-aged individuals with simultaneous cerebral symptoms. A balanced conclusion seems warranted: in symptomatic patients AF/AT for more than 8 sec may be regarded as significant arrhythmias. This has been confirmed by the recording of AF/AT simultaneously with symptoms (Paper II) or the response to therapy of these arrhythmias (Paper IV).

The SSS was detected in 3 of 77 asymptomatic, and in 6 of 26 symptomatic individuals. This difference is significant ($p < 0.02$). Furthermore, all asymptomatic cases of the SSS had ultimate evidence of sinus node dysfunction with the finding of sino-atrial block 2° in one, and advanced bradycardias in two subjects. Thus the criteria defined for the SSS may be regarded as valid when the present equipment and screening procedures were used. This conclusion is supported by the finding that among a series of 254 patients with LTER documented episodic SSS (14) according to the criteria currently used the annual risk of cerebral embolization was 7% per patient irrespective of the severity of the bradycardia.

A regular sinus bradycardia of 41-50 bpm at the time of night sleep was found in 20 (26%) of the asymptomatic individuals. Characteristic of these subjects was the absence of other complex arrhythmias. Thus, a regular sinus bradycardia with rates as low as 41 bpm during sleep may be regarded as a normal phenomenon that must be differentiated from the SSS. Camm et al (15) made similar observations of the commonness of sinus bradycardia during sleep among aged but healthy individuals. They noted, however, that sinus arrhythmia was unusual, as was sinus bradycardia when awake. This is in agreement with the present study.

Atrio-ventricular block 2° or 3°: Three of the 26 symptomatic and none of the 77 asymptomatic individuals had AVB 2° or 3° ($p < 0.05$). No instance of a single beat blocked at the atrio-ventricular level was discovered among more than 6 million beats screened among the asymptomatic individuals. Consequently, even mild and short episodes of AVB 2° are to be regarded as significant arrhythmias.

Ventricular arrhythmias: Infrequent or moderately frequent VPCs were detected in 30% of the asymptomatic individuals, i.e. they are to be regarded as normally occurring insignificant arrhythmias. Frequent VPCs were almost equally common in symptomatic and asymptomatic subjects, 8 - 5%, respectively. The difference was that they occurred in symptomatic individuals together with potentially dangerous forms according to the Lown classification (10). It may, therefore, be concluded that frequent VPCs with potentially dangerous forms are significant arrhythmias. Whether the significance of the arrhythmia is due to the frequent

occurrence in a symptomatic subject or in the simultaneous presence of potentially dangerous forms is still uncertain. Frequent VPCs, hence, also without alerting forms may constitute a significant arrhythmia in a symptomatic individual.

Comparison with previous reports: Several investigations, some having more or less epidemiological character, have demonstrated that almost every asymptomatic individual will have some kind of arrhythmia when LTER is applied (15-22). Sinus bradycardia and arrhythmia are especially common in the young (16, 17), but uncommon in the aged (15). The overwhelming majority of middle-aged or elderly individuals will show ectopic activity. This may easily lead to the assumption that all such arrhythmias demonstrated by LTER are innocent and normally occurring. Follow-ups supporting such a view are largely missing, but the few studies with follow-ups have shown that some of the "normally" occurring arrhythmias may have serious prognostic implications. An increased mortality was shown by Hinkle et al (23) even in mild daytime sinus bradycardia. Pool et al (22), Hinkle (24), and Stern et al (25) have demonstrated an increased mortality among subjects with LTER-diagnosed ventricular arrhythmia.

With one exception (21) and in contrast to the more epidemiological studies, clinically active groups have found that really serious arrhythmias were uncommon in apparently healthy elderly individuals (15, 22, 26, 27). This series has confirmed that really serious arrhythmias are common in symptomatic individuals, but uncommon in asymptomatic individuals. An as strict as possible distinction between significant and insignificant arrhythmias could be established by comparing both groups of subjects. However, the specific criteria of significant arrhythmias as derived from this study are essentially limited to the currently used LTER equipment and screening procedures.

Prediction of cause of syncope/dizziness by strictly defined significant arrhythmias (Paper II)

A routine 24-hour LTER was obtained in 81 patients with suspected Adams-Stokes syndrome. Comparisons were made with the recordings made during symptoms in 43 patients. In 38 patients who failed to develop symptoms during the recording, the routine 24-hour recordings were compared with recordings prolonged to 48 hours.

Patients with symptoms: Several investigations (12, 22, 27-43) have demonstrated that serious episodic arrhythmias are present in up to three quarters of symptomatic patients examined by LTER. Virtually all of them used patient diaries, but fewer report their experiences with diaries or similar arrangements. Those doing so have reported temporal relationships in 20%-73% of their patients although one group found it in only 9% of their patients (42). This group (21)

had previously reported that 10 (77%) of 13 apparently healthy elderly individuals had significant arrhythmia. Their failure to demonstrate temporal relationships between arrhythmia and symptoms may be illustrative: a wide definition of significant atrial ectopic beats to which the Lown criteria of ventricular ectopics were applied was used in combination with too strict criteria of bradycardias. The lack of temporal relationships between significant arrhythmias and symptoms may be explained by the definition of significant arrhythmias used. It would seem logical that arrhythmias normally occurring in healthy elderly individuals should not be expected to be the cause of symptoms and therefore not be timed with symptoms.

This study used strict criteria of significant arrhythmias derived from elderly subjects selected at random. The value of these criteria was obvious. Among patients with significant arrhythmias during a routine 24-hour LTER 15 (71%) of 21 could be confirmed as the cause of symptoms. In 6, the Adams-Stokes' syndrome was initially ruled out, but 4 of these later responded well to therapy, leaving some doubt as to the adequacy of their diaries. Thus, a total of 19 (90%) of 21 initial recordings suggesting a significant arrhythmia as the cause of symptoms could either be demonstrated or anticipated. Also, in patients with routine 24-hour recordings suggesting no cardiac cause of symptoms by revealing no significant arrhythmias, similar results were obtained. Twenty-two patients had no significant arrhythmias initially and this was confirmed by the recording of a normal cardiac rhythm during symptoms in 20 (91%).

Several investigators have observed difficulties in obtaining adequate diaries (31, 37, 41, 43) and it has been pointed out that failure to report symptoms or the incorrect timing of events (39) may falsely lead to the ruling out of the Adams-Stokes' syndrome. With the use of strictly defined significant arrhythmias we observed that ruling out of Adams-Stokes' syndrome was not definitely warranted when symptoms and significant arrhythmias did not coincide. It is obvious that diaries may have drawbacks and that they should be interpreted with caution.

Significance of frequent VPCs and atrial tachy-arrhythmias

Frequent VPCs without potentially dangerous forms and atrial tachyarrhythmias ≥ 120 bpm and lasting for more than 8 sec were equally common in subjects with and without symptoms (Paper I). The significance of these arrhythmias in symptomatic patients was evidenced by the recording of these arrhythmias during symptoms (Paper II).

Increase in significant arrhythmias by prolonged LTER in patients without symptoms during recording

Among the 38 patients in whom symptoms failed to develop, 19 had a detectable significant arrhythmia within 24 hours of recording. By prolongation of LTER from 24 to 48 hours, one additional patient had a significant arrhythmia and, again, this was an atrial tachy-arrhythmia. Thus, 95% of patients without symptoms during LTER but having significant arrhythmias were recognized within 24 hours, the same type of significant arrhythmia being present during both 24-hour periods. Therefore, the use of a routine 24-hour LTER had a fair reproducibility as regards the detection of significant arrhythmias versus no significant arrhythmias. On the other hand, 3 (18%) of the 17 patients with significant arrhythmias other than ventricular ones had additional significant ventricular arrhythmias detectable during the second 24-hour period. In patients who fail to have symptoms during the recording it must be kept in mind that a not-negligible fraction of patients with already diagnosed significant arrhythmia may have other types of arrhythmia if the recording is prolonged. However, when the initial recording is negative, the chance of finding a significant arrhythmia by prolongation is small, but AF/AT or significant ventricular arrhythmia may be found. As regards the increased yield of significant ventricular arrhythmias, our results are consistent with the findings of Kennedy et al (44). With respect to all types of arrhythmias, the currently used classification allowed fewer arrhythmias to be discovered by repeated recordings than observed by Goldberg et al (31). A further interesting observation was that no less than 19 of 20 cases with bradycardias were detected within 24 hours. This is a finding not necessarily in contrast to the report by Izivoni and Stern (45) that 7 of 12 patients with bradycardias severe enough to require pacemaker implantation were detected within 24 hours. When 12 hours of LTER was compared to 24 hours, however, Jonas et al (37) observed a considerable increase of pertinent arrhythmias.

Frequency and distribution of significant arrhythmias in suspected Adams-Stokes' syndrome (Paper III)

Among 330 patients with suspected Adams-Stokes' syndrome 173 (52%) had significant arrhythmia, a figure which could be compared with the range in the order of 20-75% reported by other investigators (12, 22, 27-43). Bradycardias were observed in 97 (29%), the SSS being more common than AVB $2^0/3^0$ - 68 and 29 cases, respectively. Tachy-arrhythmias were observed in 76 (23%) of the patients. The proportion of patients with the SSS may appear high, but other investigators using LTER also have reported that more patients with the SSS than AVB $2^0/3^0$ are

found (30, 32, 33, 38, 39, 43). This could be explained either by an increased awareness of the disorder or the LTER technique being especially suitable for the detection of the SSS. The dominance of bradycardias in the present study may in fact be the result of a special interest in bradycardias influencing internal referral patterns since other authors have reported that tachy-arrhythmias are most common in their series (12, 30, 32, 39, 41, 43).

Significant arrhythmias in relation to age and sex: In patients with suspected Adams-Stokes syndrome no less than 78% of those aged 80 years or more, but also 18% of those aged 17-39 years, had significant arrhythmias. Although the fraction of patients with a positive finding of significant arrhythmias increased with age, it must be concluded that even early age is no reason to withhold LTER once a cardiac origin or symptoms is suspected. The reports of Goldreyer et al (13) and Schott et al (46) are consistent with this conclusion.

Significant arrhythmias in relation to cerebral symptoms: The typical patient with significant arrhythmia had experienced both syncope and dizzy spells. However, 12 of 37 patients with two or more syncopal attacks, but no dizzy spells, had significant arrhythmia. Thus, a history of syncopal attacks but no dizzy spells cannot reduce the probability of significant arrhythmia enough to justify the exclusion of such patients from the benefits of diagnostic LTER.

Forty-two patients without, and 17 patients with significant arrhythmia had an earlier interpretation of epilepsy. Although the difference is significant ($p < 0.001$) a previous diagnosis of epilepsy cannot be used to exclude significant arrhythmia with reasonable accuracy. That cardiac arrhythmias may masquerade as epilepsy was recently stressed by Schott et al (46), a finding consistent with the common misinterpretation of epilepsy in patients later paced (9, 47).

The majority of patients previously interpreted as having cerebral atherosclerosis had significant arrhythmia. Thirteen per cent of patients with significant arrhythmia experienced symptoms only when rising or standing. It is obvious that the Adams-Stokes' syndrome cannot be excluded or even considered unlikely in patients having histories suggesting other causes of syncope and/or dizziness.

Paroxysmal fatigue was an outright complaint among patients with, as compared with patients without, significant arrhythmias. It might be advisable to incorporate this complaint into the list of symptoms more or less typical for the Adams-Stokes' syndrome.

In summary: Subdividing the various types and histories of syncope and/or dizziness may influence the chance of finding significant arrhythmias to a limited extent. Nevertheless, there was no typical clinical setting for patients without significant arrhythmia. Also, previous diagnoses of epilepsy and

cerebral atherosclerosis were frequently misleading and histories suggesting hypotension were unreliable. It is therefore concluded that all patients with syncope, including epileptiform types and/or dizziness, should be subjected to LTER irrespective of previous diagnoses once the Adams-Stokes' syndrome is suspected.

Significant arrhythmias in cardiac complaints: A "fast" cardiac rhythm was experienced by rather similar proportions of patients with and without significant arrhythmia, respectively. Moreover, equal proportions of patients with a history suggesting tachy-arrhythmia had tachy- and brady-arrhythmias, respectively during LTER. An "irregular" cardiac action or a "slow" pulse was noted by several patients without significant arrhythmia. Although significantly more patients with significant arrhythmias had complaints of arrhythmia, it must be concluded that an experience of a cardiac arrhythmia is no absolutely reliable indication that significant arrhythmias will be detected. Not even the type of any possible arrhythmia can be predicted. This lack of correlation between subjective cardiac complaints and arrhythmias has been previously pointed out by Kunz et al (48) and Zeldis et al (43) who recorded the cardiac rhythm during symptoms.

Significant arrhythmias and cardiac findings: The objective cardiac data provided the best prediction of significant arrhythmias. Twenty-two of the 25 patients with a history of previous digitalis-induced arrhythmias with reversal of their arrhythmia when the drug was omitted had significant arrhythmias during LTER. Among patients treated for cardiac failure almost three fourths had significant arrhythmia during LTER. Patients with a recent ECG showing permanent AF, a bradycardia of 55 bpm or less or ectopic beats had significant arrhythmias in the overwhelming majority of cases. Bundle branch blocks were found in rather similar proportions of patients with and without significant arrhythmias, respectively. Interestingly, 10 of the 30 patients with bundle branch block and significant arrhythmia had tachy-arrhythmias while monitored, a finding similar to those of DePasquale and Bruno (49) and Dhingra et al (50) and also to the observation that patients with prolonged His-to-ventricle intervals frequently have ventricular arrhythmia if monitored during symptoms (51).

Significant arrhythmias in demented patients (Paper V)

Among 32 patients widely diagnosed as having postapoplectic dementia 20, and among 17 patients with chronic psychiatric disorders in the stage of terminal dementia 6 had serious arrhythmias. Comparison of the 26 definitely significant arrhythmia cases among the demented with the elderly unselected population (Paper I) yields a significant difference ($p < 0.005$).

The arrhythmias correlated well with previous symptoms possibly due to episodic arrhythmia such as fractures, epilepsy or "strokes" without focal neurological signs. In a later study, (52) 35 demented patients in nursing homes were examined with 24 hours of LTER, 8 of them having serious arrhythmias. Typical for the demented patients in nursing homes was the combination of complete disorientation with an excellent physical health.

The difference between demented patients with physical incapacity requiring hospitalization and demented patients without physical incapacity is significant ($p < 0.02$). This does not, however, exclude a possible role of serious episodic arrhythmias in the development of dementia. Murray (53) reported several cases of "depressed mental function", Dalessio et al (54) "chronic encephalopathy", and Greene and Moss (55) "associated deliriums", accompanying bradycardia and successfully reversed by pacing. Lagergren (56) observed mental impairment when the cardiac rate in paced patients was lowered. Corday and Irwing (57) observed delirium caused by very frequent VPCs. Other studies (13, 57-62) have shown that various cardiac arrhythmias may have drastic effects on central hemodynamics and cerebral blood flow. Sulg et al (60) were able to show an increase in the mean frequency of the dominant rhythm of the ECG following the onset of pacing in bradycardic patients. Although the physiological prerequisites for a possible role of episodic cardiac arrhythmias in the development of dementia seem to be present, prospective studies may be needed to determine the exact extent - if any - to which this occurs. An editorial in the Lancet (63) suggested joint research by cardiologists and psychiatrists to determine whether the cause of dementia was within the brain or elsewhere. The title of the editorial was Cardiogenic Dementia.

Significant arrhythmias in patients with femoral neck fractures (Paper VI)

Among the 58 patients with femoral neck fractures, 23 (40%) had significant arrhythmias. This differs significantly from the asymptomatic individuals reported in Paper I ($p < 0.001$).

Fracture of the femoral neck is a stressful condition possibly capable of triggering arrhythmias. Arrhythmia then would be a result rather than the cause of trauma. However, about two thirds of patients with as compared to one third of patients without significant arrhythmia had a history of syncope and/or dizzy spells prior to the fracture event. It cannot be excluded that this difference to some extent is caused by pre-existing arrhythmias. Furthermore, since patients with significant arrhythmia had an increased mortality and an increased need for institutional care, it might be argued that even if the fracture caused the arrhythmia in some cases, this tendency might nevertheless be inherent with

the patient and, regardlessly, resulting in a poorer prognosis. This is in agreement with the study by Ceder (64) which demonstrated that arrhythmia in the standard admission ECG of patients with fracture of the femoral neck had prognostic implications.

Patients with episodic arrhythmia have a trauma incidence being twice that of matched controls (65). To the author's knowledge, there exists no investigation in which elderly patients with trauma were subjected to cardiac monitoring for the detection of explanatory occult arrhythmias. Rodstein and Camus (66) recorded the ECG immediately after accidents and compared it with available recordings prior to the event. Among their 107 patients, 24 had arrhythmias, 14 of them being present before the accident. Livisley and Atkinson (67) found arrhythmias in 35 of 57 elderly patients with unexplained accidents and concluded that cardiac arrhythmias are frequent causes of accidents in old age.

Atriopathic arrhythmias in non-hemorrhagic stroke (Paper VII)

Among the 86 patients with non-hemorrhagic stroke, atriopathic arrhythmias, i.e. permanent AF/AT, episodic AF/AT irrespective of duration and the SSS, were observed in 38 patients. Twenty-one of them had the SSS and 17 had permanent or episodic AF/AT. This differs significantly from the elderly population, selected at random (Paper I).

Permanent AF, with or without valvular disease, is a well recognized cause of cerebral embolism (68-72). In a recent Swedish series, 19 of 100 patients with acute cerebrovascular disease were considered to have cerebral embolism (73). In addition to generally-accepted causes of cerebral embolism, however, the SSS must be taken into account. This disorder is highly linked with cerebral embolism, irrespective of whether paced or not (74-76). It is obviously sufficient for the arrhythmia to be only episodically present, since patients with episodic SSS have been found to have a high incidence of cerebral embolism, 9.7% and 5.3% per patient and year in the BTS and in purely bradycardic SSS, respectively (14).

It could, therefore, be postulated that the common group of atriopathic arrhythmias - permanent and episodic - is a frequent cause of non-hemorrhagic stroke. This study confirmed that atriopathic arrhythmias were common in non-hemorrhagic stroke - 44% - when LTER is applied. This is, however, not definite evidence that the atrial disorders actually caused the strokes. Cerebral damage may result in cardiac arrhythmias; an excellent review on this subject was given by Weidler (77). However, in the Malmö series of episodic SSS (14), the arrhythmia was documented prior to the stroke and 6 of 30 patients with episodic SSS subjected to autopsy were found to have mural thrombi in the left heart. Wolf reported an almost six-fold increase in stroke following the onset of

chronic AF in patients without valvular disease in the Framingham study (72). Recently, Easton and Sherman (78) extensively reviewed the literature and concluded that the role of cardiac embolization in stroke was probably underestimated at present. They even suggested studies utilizing the LTER (the present study was then already performed). In this series, 13 of 16 patients with histories of multifocal strokes were found to have atrio-pathic arrhythmia, a finding consistent with a central source of embolization rather than several sources of artery-to-artery embolization. When angiographic studies revealed an appropriately located vascular lesion, atrio-pathic arrhythmias were infrequent. Lavy et al (79) monitored patients with acute stroke and compared the findings with previously recorded routine ECGs when available, finding that 11 of their 43 patients with non-hemorrhagic stroke had arrhythmia prior to the stroke. Goldstein (80) found that AF in stroke patients was frequently known prior to the stroke. Friedberg et al (81) compared stroke patients with age- and blood pressure-matched controls with the finding that the major difference between controls and stroke patients was arrhythmia and digitalis therapy. Hence, a major role of atrio-pathic arrhythmias in producing stroke must be concluded. LTER offers an excellent tool for the evaluation of these patients. In addition, primary prevention of stroke may be possible if episodic atrio-pathic arrhythmias have been detected by LTER.

Effectiveness of treatment of episodic significant arrhythmias (Paper IV)

The 173 patients of 330 with suspected Adams-Stokes' syndrome (Paper III) who had significant arrhythmias were reviewed after 3-5 (mean 4) years. The effect of therapy was evaluated principally by reviewing the case records as regards the possible improvement of symptoms attributable to the Adams-Stokes' syndrome. In addition, deaths and long-term need for permanent geriatric care was evaluated.

Therapy versus no therapy and symptoms of arrhythmia: Fifty-three of the 65 patients treated for brady-arrhythmias responded well to treatment of their arrhythmias with improved symptoms of syncope and/or dizziness. Subjective assessments of pacemaker therapy have shown similar results (9, 82, 83, 84). Fifty-six of the 62 patients treated for tachy-arrhythmias had improved symptoms, a result similar to previous reports (12, 32). However, 8 out of 30 patients not treated for brady-arrhythmias recovered spontaneously as compared with 1 out of 14 patients who received no treatment of tachy-arrhythmias (N.S.).

Symptoms of dizziness are vague and very common in individuals aged 75 years or more (85). It is therefore obvious that non-cardiogenic dizziness and serious arrhythmia may coexist. Symptoms may persist even in paced patients (86). Recording of the cardiac rhythm during symptoms was then needed to provide ultimate

evidence that symptoms are definitely caused by an arrhythmia. Despite this the simple classification of arrhythmias as significant with subsequent therapy was useful in the majority of cases to which it was applied.

Deaths and autopsy findings

The one year mortality of patients with permanent AVB 3⁰ as diagnosed by the standard ECG was in the order of 50% in the study by Johansson (2), but when cardiac pacing is applied survival returns to almost normal (87-90). Recently, however, Edhag and Swahn (91) found a more favourable prognosis among selected patients with AVB 3⁰ who were not paced. European centers (92,93) reported a favourable prognosis for patients paced due to the SSS but American investigators (94, 95) have observed an increased mortality in patients paced for the SSS. The American series, however, contained fewer patients followed for shorter periods. It is known that the mortality of the unpaced SSS is low both when permanently (96) or episodically present (97).

The annual mortality of patients with bradycardias was in the order of 8-10% for those actively treated and in the order of 13% for those not actively treated. Similar results were obtained in patients with tachy-arrhythmias. This moderate excess mortality, however, may in part be explained by the deaths caused by non-cerebral systemic embolization or possible systemic cerebral embolization. It appears that the risk of possible systemic embolization constitutes a greater hazard to patients with episodic significant arrhythmia than the risk of dying suddenly. A further indication of the role that might have been played by systemic embolization is the finding of encephalomalacias in 28 patients and possible non-fatal non-cerebral embolizations in 16 patients.

Long-term geriatric hospitalization: Despite the successful control of symptoms of syncope and/or dizziness among the patients actively treated, no less than 35 required long-term geriatric hospitalization during the 3-5 year follow-up. Patients actively treated for their arrhythmias were equally prone to admission to long-term geriatric care as those not actively treated. Hence, a factor other than the electrocardiographic severity of the arrhythmias must be sought. A division of the entire material into patients with and without atriopathic arrhythmias was therefore made with the assumption that atriopathic arrhythmias, due to their ability to produce systemic embolization, were more prone to cause long-term disability. Of the 126 patients with atriopathic arrhythmias, 31 were admitted to long-term geriatric care as compared with 4 of the 47 without atrio-pathic arrhythmia. This difference is significant ($p < 0.05$). It may therefore be suspected that the atriopathic components of significant arrhythmias with possible embolization are the real precursors of severe disability in patients with the Adams-Stokes' syndrome.

In summary, the treatment of significant arrhythmias is rewarding with respect to symptoms of dizziness and/or syncope and should always be attempted. A considerable fraction of these patients, however, may later suffer from disability possibly caused by embolization if atriopathic arrhythmias are present. Again, the atriopathic concept has proven its value, but future studies are needed to assess whether the inclusion of the atriopathic concept with prophylactic treatment will improve the long-term prospects of patients with significant arrhythmias.

General conclusions

- By comparing asymptomatic and symptomatic individuals in a cohort of randomly selected elderly individuals, it was possible to establish distinct criteria of significant arrhythmias.
- The criteria established for significant arrhythmias had a high degree of prediction when a routine LTER for 24 hours was compared with the cardiac rhythm during symptoms.
- More than half of patients with suspected Adams-Stokes', almost half of patients with recent fracture of the hip and more than half of the patients hospitalized due to postapoplectic dementia have significant arrhythmias. The difference to asymptomatic elderly individuals is striking and statistically significant for all three groups.
- Although objective cardiac findings or old age may increase and observed epileptiform types of syncope may reduce the probability of significant arrhythmia, it can never be excluded with reasonable accuracy once cardiac arrhythmia is suspected. Hence, all individuals with clinical complaints consistent with the Adams-Stokes' syndrome ought to be entitled to LTER.
- Treatment of significant arrhythmias is rewarding with respect to symptoms immediately related to cerebral ischemia caused by arrhythmia but will not prevent long-term disability as reflected in the need for permanent geriatric hospitalization.
- Patients with the Adams-Stokes' syndrome may be separated into two groups - those with and those without atriopathic arrhythmia. Among the former the risk of later geriatric hospitalization is significantly increased, possibly due to the association of atriopathic arrhythmias to systemic embolization.

- Almost half of patients with non-hemorrhagic stroke have atriopathic arrhythmia; the LTER provides an excellent tool for the diagnosis and work up of such patients.
- The combined role of atriopathic arrhythmias as the cause of both Adams-Stokes' attacks and systemic embolization was impressive. Future studies may hopefully show if the incorporation of the atriopathic concept in the management of patients with significant arrhythmias will improve the results obtainable by cardiogenic neurology.

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FREQUENCY AND DISTRIBUTION OF LONG-TERM ECG-RECORDED CARDIAC ARRHYTHMIAS IN AN ELDERLY POPULATION

With Special Reference to Neurological Symptoms

by

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Introduction

During the past two decades, awareness of permanent or episodic bradycardias has steadily increased. In 1966, Johansson (23) reported 63 new cases of third degree atrioventricular block (AV-bl 3^0) per 10^6 inhabitants from Malmö, 38 of them spontaneous, i.e. not triggered by drugs or observed during acute myocardial infarction (AMI). When pacemakers have been in common use, pacemaker implantation rates might be substituted for AV-bl 3^0 and symptomatic bradycardias of other kinds. The highest national pacemaker implantation rate is reported from the US, where 309 new units per million inhabitants and year were calculated for 1978 (18). The corresponding figures from the Scandinavian countries vary from 58 to 181 (18). In both instances, most pacemakers were implanted because of AV-bl 3^0 .

There has also been great interest in the sick sinus syndrome (SSS) in recent years. In their survey over pacemaker candidates, Shaw and Kekwick (33) diagnosed more than 100 new instances of SSS per million inhabitants and year during their last sampling years. It has also been shown that the introduction of "cardiogenic neurology", i.e. the active diagnosis and treatment of arrhythmias in patients with neurological symptoms, will uncover a large number of previously unknown patients requiring pacemaker treatment (6).

Impressive pacemaker implantation rates reflect only part of the problem; many more patients with supposed cerebrovascular symptoms might suffer from serious episodic tachy- or bradycardias. Applying long-term electrocardiographic recording (LTER), several authors report that as much as 20-75% of patients examined because of suspected Adams-Stokes' syndrome have serious episodic arrhythmias (2, 8, 13, 17, 24, 25, 26, 28, 29, 34, 35). Seemingly in contrast with these results, epidemiological studies have shown that most young or middle-aged persons have some type of arrhythmia while being examined by LTER (9, 11, 12, 14, 21). However, the overwhelming majority had innocent types of arrhythmia and really serious arrhythmias were few. Clinical investigators looking for normal versus abnormal cardiac rhythm in selected middle-aged or elderly persons find practically no serious arrhythmias (15, 28, 32).

As far as the author knows, there is no publication in which an unselected

elderly population has been examined for the presence of episodic arrhythmias. This study determined the types and frequencies of episodic arrhythmias occurring in a randomly selected elderly population and assessed the need for treatment of arrhythmias in those with cerebral symptoms.

Methods

Study population

A consecutive series of suspected Adams-Stokes' syndrome patients referred to the author over two years was available (2). For each patient referred during the first year, one person with the same year and day of birth and the same sex was randomly selected by the Population Actuary in Malmö. The names of 157 persons aged 47-92 years (mean $\pm$ S.D. 71 ± 11) were given to the author; 103 were examined by LTER. One subject with AMI and one with open pulmonary tuberculosis were excluded, 52 refused or failed to attend. Fig.1 gives the age and sex distribution of those examined and those not examined by LTER.

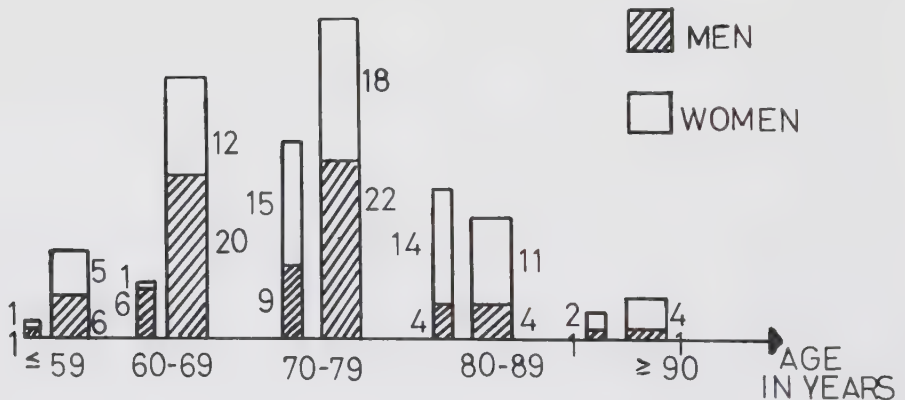


Fig. 1. Age and sex distribution of the study population. Left bar = individuals not examined by LTER, right bar = individuals examined by LTER.

Clinical and chemical examination

Each person was subjected to a careful assessment of previous diseases. His past or present cardiac or neurological symptoms were recorded. A physical examination, including a search for neurological signs, was performed. Arterial blood pressure was measured after lying for 5 min and immediately after standing up. A routine 12-lead ECG was recorded at rest. On the next morning, blood samples for the following analyses were drawn: Hb concentration, WBC, one-hour ESR, sodium, potassium, calcium, bilirubin, hepatic enzymes (ASAT, ALAT, GT, and ALP), creatinine, cholesterol triglycerides, thyroxine, and fasting blood glucose. The urine was tested for the presence of albumin and glucose. The analyses were made by the Department of Clinical Chemistry of the General Hospital, and their reference values were used in the interpretation of the results.

LTER and screening of arrhythmias

The physical examination was followed by the attachment of an ECG tape recorder type SRA/HRB-3 (Helcomed Norden/Hellige), which the person was asked to wear for 24 hours. As some subjects were unable to manage the equipment, and as some parts of the recordings could not be accepted owing to poor technical quality, the average time of available LTER was 22 hours. The minimum time of successful LTER was 12 hours in one subject and a total of 15 recordings contained 12-20 hours of usable LTER.

The ECG tapes were screened with an automatic unit. All rhythms faster than 120 or slower than 40 beats/min (bpm) as detected by single R-R interval analysis, triggered the unit to present a one-channel ECG on a paper strip. Also every 10th ventricular premature contraction (VPC) detected by configuration criteria and occurring within 1 min, triggered a write-out.

Ectopic beats were classified as follows. The highest frequency of atrial premature contractions (APCs) and VPCs was graded in sequences containing three or more ectopic beats. Infrequent: one ectopic beat in more than 10 beats. Moderately frequent: one ectopic in 6-10 beats. Frequent: one ectopic in 5 beats or less. In addition, potentially dangerous VPCs according to principles of Lowin and Wolf (27) were recorded. They were VPCs of multifocal origin, couplets (i.e. salvos of two VPCs with short intervals) and R-on-apex-T types.

A tachycardia, atrial or ventricular, contained three or more consecutive beats. Atrial tachyarrhythmias with rates of 120 bpm or more were divided into atrial fibrillation/flutter (AF) or atrial tachycardia (AT). Heart rates were measured in a sequence of three beats or more.

The SSS, whether spontaneous or triggered by drugs, fulfilled one or more

of the following criteria: 1) Sinus bradyarrhythmia ≤ 50 bpm, 2) Regular sinus bradycardia ≤ 45 bpm when awake, 3) Sinoatrial block, 4) Sinus arrests ≥ 1.5 sec. All those with SSS were referred to this group irrespective of their possible additional arrhythmias.

In atrial fibrillation, episodes of bradycardia of ≤ 40 bpm, as measured in a sequence of three beats or more, were referred to as AV-bl 3⁰.

Subjects already paced when they appeared were not examined by LTER. They were incorporated with the findings among symptomatic controls.

The definition "significant" arrhythmias refers to serious arrhythmias known to correlate with cerebral symptoms, "insignificant" to other arrhythmias.

Results

Twenty-six subjects had experienced symptoms, possibly Adams-Stokes' syndrome, during two years before the LTER: some type of dizzy spells in 18 and syncope in 8. The other 77 subjects had been asymptomatic in this respect.

Atrial tachyarrhythmias lasting for 8 sec or more were found in one of the symptomatic and 2 of the asymptomatic subjects. Frequent VPCs with couplets or R-on-apex-T types were detected in two symptomatic persons but in none of the asymptomatic. Although some of the asymptomatic controls had episodes of frequent VPCs, none had potentially dangerous forms (Table I).

Table I. Significant episodic arrhythmias in controls with and without dizzy spells/syncope

	Symptomatic (n = 26)	Asymptomatic (n = 77)	p
Atrial tachycardia of 120 bpm or more for 8 sec or more	1	2	NS
Frequent VPCs with alerting forms	2	0	NS
SSS			
Total	6	3	< 0.02
Already paced	1	0	
AV-bl 2 ⁰ or 3 ⁰			
Total	3	0	< 0.05
Already paced	1	0	
Total	12	5	< 0.001

SSS was found in 6 symptomatic and 3 asymptomatic subjects. One of those with symptomatic SSS was a patient earlier diagnosed by LTER, which revealed an SSS with additional AV-bl 2⁰. After pacemaker implantation he had had no syncopal attacks during a two-year follow-up. Two of the three asymptomatic controls with SSS had severe bradycardia of 34 and 36 bpm, respectively, and one had a typical 3:2-blocked sinoatrial block without bradycardia but lasting for minutes on several occasions (Table I).

An AV-bl 3⁰ was found in 3 symptomatic but in none of the asymptomatic controls (Table I). One was already paced. He had had several syncopal attacks before pacemaker treatment, but no further attacks during a three-year follow-up. The other two controls presented with histories of recent syncopes.

Insignificant arrhythmias (Table II)

Table II. Insignificant episodic arrhythmias in 77 controls without dizzy spells/syncope

Arrhythmia	N	%
APCs		
Infrequent	42	55
Moderately frequent or frequent	15	19
Atrial tachycardias of ≥ 120 bpm for ≤ 8 sec	7	9
VPCs		
Infrequent	21	27
Moderately frequent or frequent	6	8
Regular sinus bradycardia during night sleep (bpm)		
41-45	3	4
46-50	17	22

Most of the 77 controls without dizzy spells or syncope had some kind of insignificant arrhythmia. Infrequent APCs were observed in 42 of them; 15 had moderately frequent or frequent APCs. VPCs were infrequent in 21 and moderately frequent or frequent in 6 of the asymptomatic controls. It is noteworthy that no single "alerting" VPC was detected among the asymptomatic subjects. It is also remarkable that none of the asymptomatic controls ever had a single regular beat that was blocked at the atrioventricular level.

During night sleep, a perfectly regular sinus bradycardia with rates of 41-45 bpm was found in 3 subjects, whereas 17 had sinus bradycardias with rates of 46-50 bpm.

Cardiac and neurological symptoms and findings
in relation to arrhythmias (Table III)

Table III. Cardiac and neurological symptoms in relation to significant arrhythmias

	Group A (n = 12)	Group B (n = 14)	Group C (n = 77)
Normal resting ECG/no cardiac symptoms	4 (33%)	7 (50%)	57 (74%)
ECG-proven previous AMI	0	3	3
Angina			
On effort	0	0	5
Other types	3	2	7
Treatment for cardiac failure	2	4	0
Feeling of ectopic beats	6	2	7
Feeling of tachycardia	4	1	3
Cerebrovascular accidents/ positive focal neurology at examination	2	5	4

The study population was divided into three groups. Group A: 12 subjects with dizzy spells/syncope and significant arrhythmia during LTER. Group B: 14 controls with dizzy spells/syncope but without significant arrhythmia during LTER. Group C: 77 subjects without dizziness/syncope.

Cardiac symptoms: No cardiac symptoms in combination with a normal resting ECG were presented by 4, 7, and 57 subjects in groups A, B, and C, respectively. Three subjects each in groups B and C had a history of previous AMI. Angina on effort was experienced by 5 subjects in group C, other types of angina or chest pain, possibly of other origin, were noted by 3, 2, and 7 subjects in groups A, B, and C, respectively. Two subjects in group A and 4 in group B were on treatment for cardiac failure.

Six subjects in group A, 2 in group B and 7 in group C had felt an irregular heart action. Resting ECG revealed an APC in one of the group C subjects. Four subjects in group A, 1 in group B, and 3 in group C had experienced tachycardia, but none of the 103 persons in the entire study had ever noted a slow pulse.

Neurological symptoms: Cerebrovascular accidents with a focal neurological defect, or the finding of focal neurological signs at the examination, were encountered in 2 group A, 5 group B, and 4 group C subjects.

A drop in systolic blood pressure of at least 25 mmHg occurred immediately

after rising to the standing position in 2, 5, and 3 subjects in groups A, B, and C, respectively. Two subjects in group B with a history of dizzy spells had an increase of 20 bpm or more in pulse rate immediately after standing up, with a concomitant feeling of dizziness. Three subjects each in groups A and B experienced dizziness when they rose to the standing position, a phenomenon not noted among the asymptomatic subjects. Five subjects in group A and 13 in group B declared that their dizzy spells occurred only in the upright position. One of the "dizzy" subjects in group B had an advanced alcoholic ataxia.

To summarize: Only one of the 14 subjects with a history of dizzy spells/syncope but without significant arrhythmia during LTER (group B) had no explanation for the symptoms. She was later found to have intermittent confusion with digitalis selfintoxication causing severe nodal bradycardia. On the other hand, 6 of the 12 subjects with dizziness/syncope and significant arrhythmia also had a history or finding suggesting an orthostatic or hypotensive mechanism as the cause of their symptoms.

Evaluation of controls not examined by LTER
(Table IV)

Table IV. Controls not examined by monitoring

	N
Records in the Medical Department	21
No dizziness/syncope	12
One ECG	4
≥ 2 ECGs	14
Records in other departments	17
No dizziness/syncope	10
One ECG	7
≥ 2 ECGs	6
Interviewed	11
No dizziness/syncope	10
One ECG	
≥ 2 ECGs	0
Unknown	5

Efforts were made to evaluate all 54 subjects not examined by LTER. A search of the files of the record room of the Medical Department revealed that 21 persons had a record less than two years old. Personal interviews and searches traced a further 17 who had records in other departments of the General Hospital. Moreover, 11 subjects without a file in any department were assessed by personal interviews. This left 5 subjects unassessed: all 5 were alive one year later, and none of them had been hospitalized at any hospital in Malmö

since 1974. Thus a total of 49 of 54 controls not examined by LTER could be assessed with regard to cardiac and neurological symptoms.

Fraction of controls with dizziness/syncope examined and
unexamined by LTER

Fig. 2 gives the percentage of LTER-examined controls with dizziness/syncope in relation to age compared with the invited but not examined controls. The differences were slight within the respective age decades, but there was an age-related increase in the percentage of individuals who had experienced dizzy spells or syncope.

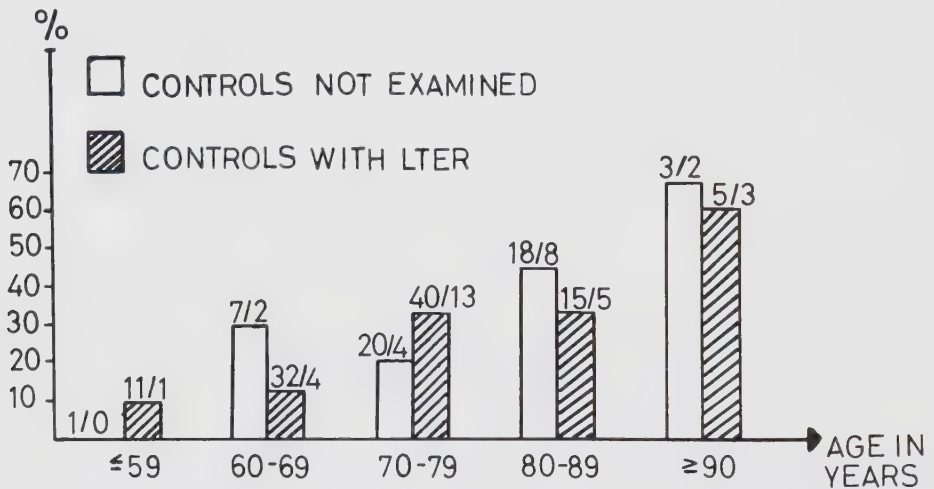


Fig. 2. Percentage of controls with a history of recent dizziness or syncope in relation to age. The fractions indicate total no. of controls/no. of controls with dizziness or syncope.

Documented arrhythmias before intended LTER (Table V)

All routine resting ECGs not older than two years and all possible LTERs were scrutinized for arrhythmias among the 49 traced drop-outs and compared with the ECGs of the actively examined 103 subjects.

One or more resting ECGs were available for 29 of the 49 traced drop-outs. SSS was present, according to the criteria given previously, in 3 drop-outs and 2 LTER-examined subjects. One subject in each group had had the SSS diagnosed by previous LTER because of suspected Adams-Stokes' syndrome. The patient

in the actively examined group was successfully paced for his bradycardia. Symptomatic AV-bl 3^0 was present and successfully paced in one of the 103 active participants and in 2 of the 49 traced drop-outs, one of whom was already successfully paced. Permanent atrial fibrillation was detected in one of the 103 subjects examined and in 2 of the 49 traced drop-outs. Paroxysmal atrial fibrillation was documented in one of the drop-outs; 6 subjects had had VPCs and 3 APCs at some ECG recording during the past two years, the corresponding figures for the drop-outs being 1 and 1 (Table V).

Table V. Arrhythmias documented by resting ECG or (when performed) monitored ECG before the present investigation

	103 monitored persons	49 monitored persons
Persons with resting ECG	103	29
Previous monitoring	1	1
SSS		
Total	2	3
Already paced	1	0
AV-bl 2^0 or 3^0		
Total	1	2
Already paced	1	1
Atrial fibrillation		
Permanent	1	2
Paroxysmal	0	1
VPC	6	1
APC	3	1

It was noteworthy that two of the unexamined persons with SSS were permanently treated in a geriatric hospital. Both were considered to have sequelae following repeated falls with cerebral concussions. The other subject unexamined by LTER, who had SSS according to the resting ECG, had been on drug treatment for epilepsy without success. The not paced patient with AV-bl 3^0 among the drop-outs was in permanent geriatric care for cardiac failure and excessive tiredness. This patient was interpreted as a case of "stable atrial fibrillation", the true nature of the condition being undiscovered.

Clinical outcome
Conditions other than cardiovascular (Table VI)
 Table VI. Non-cardiovascular conditions treated

	No. of pats.
Hypothyrosis	1
Thyroid adenoma, autonomous	1
Diabetes mellitus onset	1
Folic acid deficiency	1
Folic acid and vitamin B ₁₂ deficiency	1
Pathological hepatic enzymes	5
Lung cancer	1
Polyps of the colon	2
Inguinal hernia	1
Hydrocele testis	1
Benign gastric ulcer	1
Urinary tract infection	3

The study included a general medical check-up that disclosed various non-cardiovascular conditions in 19 of the 103 LTER-examined subjects.

Hypothyrosis, autonomous thyroid adenoma, and diabetes mellitus of recent onset were found in one woman each. Two persons with diffuse tiredness and discrete signs of neuropathy had folic acid deficiency, one of them in combination with vitamin B₁₂ deficiency. In both, the symptoms were abolished by substitution therapy. In 5 instances, pathological hepatic enzymes were detected. All of them admitted heavy drinking, but one man without abdominal symptoms who had an isolated elevation of GT died four months later from metastatic cancer of the pancreas. One subject had cancer of the lung. Two persons with bowel symptoms were found to have benign polyps of the colon. Two patients were referred to the Department of Surgery because of benign conditions: one had hydrocele testis and the other inguinal herniation. One person with gastric complaints had gastric ulcer, which was found to be benign at gastroscopy and biopsy. Three subjects were treated for symptomatic urinary tract infections.

Cardiovascular conditions (Table VII)

Table VII. Cardiovascular conditions treated

	No. of pats.
Hypotension, medicated	2
Hypertension, medicated	3
Atrial tachyarrhythmias, medicated	2
Ventricular arrhythmias, medicated	2
Digitalis withdrawn due to brady- cardia	3
β -blocker withdrawn due to brady- cardia	1
Pacemakers offered	3
Angina pectoris	
Medicated	2
Coronary bypass	1

In 19 instances, action due to cardiovascular conditions was considered indicated.

In two persons, severe and symptomatic hypotension was medicated; relief of symptoms occurred in both. Moderate hypertension was detected in three, who received treatment and were followed.

Atrial tachyarrhythmias were treated by drugs in 2 subjects who had chest discomfort caused by the arrhythmia. Both the subjects with ventricular arrhythmia and dizzy spells were given antiarrhythmic treatment, which abolished the symptoms.

Digitalis was withdrawn in three controls. Two had SSS, one of them with cerebral symptoms, and one had AV-bl 3^0 . A β -blocker was withdrawn in one subject with SSS. Thus drugs triggering bradycardias were withdrawn in 4 controls. Re-examination by LTER showed restoration of normal cardiac rhythm after withdrawal of these drugs.

Two persons with severe symptomatic and not drug-induced sinus bradycardia of less than 40 bpm and one subject with spontaneous and symptomatic AV-bl 3^0 were offered cardiac pacemakers.

Thus, treatment of arrhythmias was considered indicated in 11 out of 103 elderly persons examined by LTER, 10 of them having symptoms. Four received antiarrhythmic treatment for tachycardias, medication was withdrawn in 4 due to drug-induced bradycardias, and 3 were offered pacemaker implantation, in addition to those 2 who were already paced when they appeared.

Two controls received drug treatment for angina pectoris. One underwent

coronary bypass surgery after unsuccessful medication.

Discussion

Proportion of those with significant arrhythmias in relation to cerebral symptoms

Previous reports indicate that as many as 20-75% of patients examined by LTER due to suspected Adams-Stokes' syndrome have significant episodic arrhythmias (2, 8, 13, 17, 24, 25, 26, 28, 29, 31, 34, 35). However, epidemiological studies have shown that the overwhelming majority of young or middle-aged persons have some kind of cardiac arrhythmia, as revealed by LTER (9, 11, 12, 14, 21). This seemingly suggests a similarity with the findings in elderly persons with symptoms of cerebral ischaemia. However, really serious arrhythmias were uncommon in the young and middle-aged. It also appears incorrect to compare old patients with syncopal attacks with the young and healthy.

Clinical investigators examining both symptomatic and selected healthy middle-aged or elderly controls find virtually no significant arrhythmias among the elderly (15, 28, 32).

Which episodic arrhythmias are really pathologic in old age? Turning to the findings among the asymptomatic 77 patients, some conclusions can be drawn: Despite the finding of some kind of arrhythmia in 95% of the asymptomatic elderly persons, only 6% had significant arrhythmias. Among the elderly with symptoms suggestive of periodic cerebral ischaemia, 12 (46%) had significant arrhythmias, a significant difference ($p < 0.001$). However, no fewer than 20 (26%) of the asymptomatic persons had moderate regular sinus bradycardia during night sleep and 7 (9%) had short bursts of atrial tachyarrhythmias. Obviously, in old age it is normal to have atrial tachyarrhythmias lasting for a few seconds or a moderate regular sinus bradycardia during night sleep. A few asymptomatic persons had frequent VPCs, but altering VPCs were observed only in symptomatic subjects. Consequently, it might be appropriate to accept episodes of frequent VPCs, provided the patient is free from cerebral symptoms and no altering forms are detected.

Although atrial tachyarrhythmias of ≥ 120 bpm and lasting for > 8 sec were equally common in symptomatic and asymptomatic persons, there is evidence that this type of arrhythmia should be classified as significant. A temporal relation between atrial tachycardia and cerebral symptoms was reported by Walter et al (35) and confirmed by others (5). Moreover, Goldreyer et al (19) showed an impressive haemodynamic deterioration at the onset of atrial tachycardia in middle-aged patients simultaneously with cerebral symptoms.

AV-bl 2⁰ or 3⁰ was detected in only 3 of the symptomatic subjects. This

finding is significant compared with the absence of AV-bl 2⁰ or 3⁰ among asymptomatic subjects ($p < 0.05$). It is noteworthy that among the 77 who were free from dizziness and syncope, there was not a single instance of a normal sinus beat blocked at the atrioventricular level, even though more than 6 million cardiac cycles were screened.

Lacking generally-accepted criteria for episodic SSS, it might be thought that the criteria used are too mild. However, 6 out of 9 subjects with an episodic SSS had cerebral symptoms, a significant difference ($p < 0.02$). Also the three patients with SSS without cerebral symptoms had definite signs of sinus node dysfunction: two had severe bradycardia with 34 and 36 bpm, respectively, and one had repetitive and long-lasting episodes of sinoatrial block. All those with SSS and all with high degree AV-bl were re-examined by LTER, which confirmed the bradycardias. Furthermore, the inclusion of subjects with possible regular sinus bradycardia of 51-55 bpm when awake or with sinus bradyarrhythmia of 46-50 bpm would not increase the number of those with the diagnosis of SSS in the present study. Also in the Malmö series of episodic SSS, patients with mild bradycardia did not have a better prognosis (3) or a lower risk of cerebral embolism (4) than patients with serious bradycardia. This view of mild sinus bradycardia is supported by the report of Hinkle et al (20). They followed middle-aged men with a moderate or "relative" sinus bradycardia and found an increased risk of death during follow-up, despite the absence of ischaemic heart disease. They concluded that mild sinus bradycardia was a sign of intrinsic disease of the cardiac pacemaker.

Cardiac arrhythmias in the elderly

Subjects with indications for treatment of arrhythmia

The number of subjects having dizzy spells or syncope may seem high but others have reported similar figures (30). The finding of significant arrhythmia in 46% of them is reasonable compared with previous reports (2, 8, 13, 17, 24, 25, 26, 28, 29, 34, 35). It is unlikely that the relatively large number of drop-outs has influenced the results, as the fractions of symptomatic subjects and of subjects with previously ECG-documented significant arrhythmias are equal in the actively examined group and among the drop-outs.

As a result of this study, 11 of the 103 elderly persons studied were recommended treatment for cardiac arrhythmias. Drugs were withdrawn or instituted in 8 subjects; 7 of them had cerebral symptoms which were thereby abolished. Pacemakers are offered in Malmö to patients with spontaneous AV-bl 3⁰ and to patients with spontaneous bradycardia of ≤ 40 bpm or less in SSS, provided they have symptoms. Based on these indications, 3 of the 103 randomly

selected elderly persons were offered pacemaker treatment in addition to those two who were already paced when they appeared. These criteria for cardiac pacing are strict and in accordance with the recommendations of an international expert panel (22). It can be added that none of the five who fulfilled the criteria for pacing had obvious contraindications as revealed by the extensive, general examination; also that one subject with severe sinus bradycardia and frequent Adams-Stokes' attacks refused pacemaker therapy. As a result of the study, she was diagnosed as having latent hypothyroidism; thyroxine substitution unexpectedly abolished both bradycardia and faintings.

Widening the indications for pacemaker therapy to include also still asymptomatic cases of SSS with severe bradycardia would have increased the number of subjects to be paced to 7. And if those still asymptomatic with a mild SSS, those treated by withdrawing drugs that trigger bradycardias, and those with bifascicular disease are to be considered possible future pacemaker candidates, the hypothetical figure of pacemaker patients, present and future, would increase to at least 12 of the 103 randomly selected elderly persons.

Cardiac pacing may seem expensive and even in some instances hazardous. However, most subjects with significant arrhythmia in this study needed only conservative management. If the alternative to active treatment of arrhythmias is chronic institutional care, this is a far heavier burden on the community. In a study from Malmö (10), the demand for institutional care was estimated at 7% of the population aged 70 years or more. There is reason to believe that some patients with undiagnosed significant arrhythmias are in permanent hospital care, interpreted as having other aetiologies of their disability. In a psychogeriatric hospital, 20 out of 32 patients treated for "post-apoplectic" dementia in a broad sense had significant episodic arrhythmias (1). The arrhythmias correlated well to previous fractures or syncopal attacks. Also patients with femoral neck fracture have an increase in significant arrhythmias (7). Although the ultimate evidence that an arrhythmia is the cause of symptoms might require the establishment of a temporal relation between arrhythmia and symptoms, almost half of the symptomatic subjects had significant arrhythmias compared with a few of the asymptomatic subjects.

Hopefully, future studies will show whether a large-scale attempt to detect and treat such significant arrhythmias will enable an increasing number of the elderly to enjoy a life free from episodic cerebral ischaemia and to remain in their own homes. Neither should one overlook the humanitarian aspects. Green and Moss (16) studied the psychological adjustment to pacemaker treatment and concluded that the cardiac pacemaker provided a much more concrete basis on which to rely than the nebulous fate of old age.

Acknowledgement

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PREDICTIVE UTILITY OF ROUTINE 24-HOUR ELECTROCARDIOGRAPHY IN SUSPECTED ADAMS' STOKES' SYNDROME - COMPARISON WITH THE CARDIAC RHYTHM DURING SYMPTOMS

by

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Abstract

Using strictly defined criteria of significant arrhythmia, long-term electrocardiographic recording (LTER) has been evaluated for confirmation of arrhythmias as the cause of cerebral symptoms in 81 patients with suspected Adams-Stokes' syndrome.

Extension of LTER for more than 24 hours gives marginal additional information at a high cost. Among 43 patients monitored until symptoms, non cardiogenic causes could be ascertained in 20 of 22 patients by the recording of a normal rhythm during symptoms. Fifteen of 21 patients with significant arrhythmia during an asymptomatic 24-hour recording later had the same arrhythmia during symptoms.

Of 38 patients who failed to develop symptoms, 21 had significant arrhythmia detectable within 24 hours and 23 when 48 hours of recording was analysed.

Introduction

Long-term electrocardiographic recording (LTER) has revealed that in the order of 20-75 per cent of patients with suspected Adams-Stokes' syndrome have serious arrhythmias known to or presumed to correlate with cerebral symptoms (1-22). The varying rates of positive findings might be explained by differences in patient selection. Variations in duration of LTER and criteria for serious arrhythmias should also be considered. Lopes et al (23) observed a moderate increase in ectopic beats while Jonas et al (13) observed an increase in pertinent arrhythmias from 14 to 23 per cent as LTER was extended from 12 to 24 hours. However, Kennedy et al (24) found that most instances of ventricular arrhythmia were correctly graded within 24 hours. Less is known about the increased detection of bradycardias as LTER is prolonged but Tzivoni and Stern (25) reported that most cases with bradycardias severe enough to require pacemaker therapy were detected within 24 hours. Prolongation of LTER until symptoms appear may establish a temporal relationship between arrhythmia and symptoms or it may rule out the Adams-Stokes' syndrome by recording a normal cardiac rhythm during symptoms.

The main objective of the present study is to compare the cardiac rhythm during symptoms with the arrhythmias detected during a 24 hour LTER using strict criteria for significant arrhythmias. In patients who failed to develop symptoms we determined the increase of serious arrhythmias detectable by prolongation of LTER from 24 to 48 hours.

Patients and methods

Patients

The study included 81 patients aged 15-86 years (mean $61 \pm$ S.D. 16) suspected of having the Adams-Stokes' syndrome. All were selected for prolonged LTER due to frequent symptoms of syncope and/or dizziness. All patients had consented to wear an ECG-tape-recorder until symptoms occurred and kept a diary noting time of symptoms. Patients unable to present adequate diaries or with recent changes in their cardiac medication were excluded from the study. An examination was performed prior to the study in order to detect possible non-cardiac causes of symptoms. All patients participated at least 48 hours but 38 patients terminated recording prior to symptoms due to subjective discomfort.

Methods

LTER

LTER was performed using portable ECG-tape-recorders type SRA/HRB-3 (Helcomed Norden/Hellige). The patients revisited the Section of Cardiology every second day for a technical check-up.

Screening of ECG-tapes

The ECG-tapes were screened by one of two automatic units. One unit writes out all rhythms corresponding to rates faster than 120 or slower than 40 beats per minute (bpm) as detected by single R-R-interval as a one-channel ECG on a paper strip. Write-out from the other unit is triggered by an increase or decrease of the cycle length of 30 per cent or more of the average from the last minute of recording. In addition, both units write out every 10th ventricular premature contraction (VPC) occurring within one minute of recording as detected by QRS configuration criteria. All ECG write-outs were screened by a specialised laboratory technician and one of the authors (N-J A).

Classification of arrhythmias

Arrhythmias known or presumed to correlate with cerebral symptoms were termed significant. Minor arrhythmias expected to occur in asymptomatic elderly individuals were classified as insignificant and omitted from this presentation.

The criteria of significant arrhythmias were based on the findings made

when 103 elderly individuals (mean age 71 ± 11 years) selected at random from the general population were examined by 24 hour LTER using the same equipment and screening limits(26). The following arrhythmias were termed significant: Frequent VPCs defined as one VPC per 5 or less cardiac cycles in a sequence containing three or more VPCs and of potentially dangerous VPCs (27) only VPC-couplets defined as two VPCs with short or no interval were considered, ventricular tachycardias containing three or more beats; atrial tachyarrhythmias at a rate of ≥ 120 bpm and duration > 8 sec, the sick sinus syndrome according to one or more of the following criteria,

- 1) Sinus bradyarrhythmia ≤ 50 bpm and with a variation in consecutive P-P-intervals of ≥ 20 per cent or more,
- 2) Regular sinus bradycardia ≤ 45 bpm when awake,
- 3) Sino-atrial block and,
- 4) Sinus arrests of ≥ 1.5 sec. The lowest heart rates were calculated from a sequence of three or more beats of the basic rhythm. Patients with the sick sinus syndrome and additional episodes of atrial tachyarrhythmias were considered to have the bradycardia-tachycardia syndrome.

Atrioventricular block 2^o and 3^o was always significant. In atrial fibrillation 3^o block was designated if the ventricular rate was ≤ 40 bpm or 41-50 bpm with an obvious escape rhythm.

Results

The 81 participating patients are divided into two groups. One group consists of 43 patients who tolerated LTER until symptoms appeared and one of 38 patients terminating LTER at varying times ≥ 48 hours but prior to symptoms. Examination continued 2-21 days (mean 4).

Patients with symptoms during LTER

Among the 43 patients with symptoms 28 had syncope or dizzy spells. In 15 patients the symptoms during recording were cardiac but often connected with a sensation of pending collapse or associated with onset of typical cerebral symptoms.

The arrhythmia diagnoses during the 24 hour periods and the number of patients with symptoms are shown in Table 1. Furthermore, patients with a normal rhythm during symptoms are shown.

During the asymptomatic period 22 patients had no significant arrhythmia. A non-cardiac cause of their symptoms could be confirmed in 20 (91%) patients who had no significant arrhythmia during the entire 24-hour period during which symptoms occurred. Two patients lacking significant arrhythmia during the

initial 24-hour period both had atrial tachyarrhythmias when symptoms later developed.

Table I. Patients examined by LTER until appearance of symptoms. Comparison of 24-hour recording with and without symptoms occurring. Arrows indicate cases with a new arrhythmia diagnosis after prolongation.

Arrhythmia	Patients with arrhythmias present during 24-hour period		Patients with normal rhythm during symptoms
	without symptoms	difference	with symptoms
No significant	22	- 2	20
Atrial tachyarrhythmias	7	+ 2 - 1	8
Sick sinus syndrome		↓	
Brady-tachy	6	+ 1	7
Bradycardia only	1	- 0	1
Atrioventricular block 3°	1	+ 0	1
Frequent VPCs	2	+ 0	2
VPC-couplets/	4	+ 0	4
Ventricular tachycardia			

Twenty-one patients had significant arrhythmias suggesting a cardiac origin during the asymptomatic period. When symptoms did appear it could be confirmed that the same significant arrhythmia previously recorded was related to symptoms in 15 (71%) of them. Furthermore, one patient with atrial tachyarrhythmia both initially and during symptoms had episodes of sinus bradycardia unrelated to symptoms during the same 24-hour period in which symptoms occurred. This allowed the correct diagnosis of a bradycardia - tachycardia syndrome.

In 6 of the 21 patients who had significant arrhythmias during the initial period, symptoms were not simultaneous with the arrhythmias. However, one of these patients later reported disappearance of cerebral symptoms after pacemaker implantation and 3 reported disappearance of symptoms on antiarrhythmic medication.

In 15 of the 17 patients with simultaneous arrhythmias and symptoms the arrhythmias observed in connection with symptoms were of the same type and severity as those previously observed during the asymptomatic period. Notable aggravations of pre-existing arrhythmias were observed in only two cases: one with VPC-couplets developed a ventricular tachycardia and one with atrioventricular

block 3⁰ had an asystole of 21 sec. as they fainted.

A new type of additional significant arrhythmia was discovered during the period in which symptoms occurred in 3 patients. They had frequent VPCs temporally unrelated to symptoms.

Patients without symptoms during LTER

(Table II)

Table II. Patients without symptoms during monitoring. Comparison of significant arrhythmias present during a 24-hour initial period and diagnosis after a second 24-hour period. The arrow indicates a patient with a new arrhythmia diagnosis after prolongation.

Arrhythmia	Patients with arrhythmias present during 24-hour period			Patients with new additional type of significant arrhythmia
	initially	difference	with 2nd period included	
No significant arrhythmia	19	- 1	18	
Atrial tachyarrhythmias ≥ 120 bpm > 8 sec.	5	$\downarrow$ + 1	6	1 (VPCs)
Sick sinus syndrome				
brady-tachy	4	0	4	1 (VPCs)
brady	4	0	4	
AV-dissociation	1	0	1	
Atrioventricular block 2 ⁰ /3 ⁰	3	0	3	1 (VPCs)
Frequent VPCs	1	0	1	
VPC-couplets	1	0	1	

Thirty-eight patients had no symptoms during monitoring. Nineteen had no significant arrhythmia during the initial 24 hour period, 18 (95%) of them remaining free from significant arrhythmias when LTER was extended to 48 hours. The one patient discovered by prolongation had atrial tachyarrhythmia, the remaining 5 patients with atrial tachyarrhythmias were discovered within 24 hours of LTER. All 8 patients with the sick sinus syndrome, all 3 with atrioventricular block 2⁰/3⁰ and both with ventricular arrhythmia were detectable during the first 24 hours of recording. However, 3 patients with significant arrhythmias during the first 24 hours had the additional finding of ventricular arrhythmia as LTER was extended from 24 to 48 hours.

Discussion

The clinical management of patients with cerebral symptoms and episodic cardiac arrhythmia has of necessity been empirical unless a temporal relationship between arrhythmias and symptoms could be established. The development of LTER enables correlation of symptoms and arrhythmia. The present study intends to establish reasonable/optimal time limits for recording using strict criteria for significant arrhythmia regardless of occurrence of symptoms, as it is often impossible to observe patients during symptomatic phases.

Arrhythmias during initial (routine) 24 hours versus recordings during symptoms

Among the 43 patients with ECG recordings until symptoms appeared, the asymptomatic period included no significant arrhythmia in 22. By recording of the cardiac rhythm during symptoms a non-cardiac cause of symptoms could be confirmed in 20. Thus with the presently used classification of significant arrhythmias a negative routine 24 hour LTER gave a 91% correct prediction that the rhythm during symptoms will be normal.

When the 24 hour recording suggested arrhythmia to be the cause of symptoms by the presence of significant arrhythmia, this was confirmed in 15 of 21 patients (71%) by recording of the same arrhythmia during symptoms. However, 4 of 6 patients with significant arrhythmias not coinciding with symptoms improved on antiarrhythmic therapy. This improvement may have been spontaneous and causality was not further investigated. Hence a routine 24 hour recording with significant arrhythmia was either confirmed or, using the terminology of Ward et al (22), clinically useful in 90% of the cases.

The clinical management of patients with significant arrhythmias is frequently based on the presumption that the arrhythmias documented are the antecedents of more serious arrhythmias. Among our 17 patients with simultaneous arrhythmia and symptoms this was only observed in 2. The remaining 15 patients rather showed a varying response to the same arrhythmia.

Three previous reports (16, 19, 22) have demonstrated temporal relations between arrhythmias and cerebral symptoms in less than 10 per cent of their patients, while others ranged from 13 to 76 per cent. A considerable number of patients have no significant arrhythmia at any time of recording including during symptoms. There is little doubt that the former deserve treatment for arrhythmia and that a non-cardiac cause should be sought among the latter. More problematic is the handling of patients with significant arrhythmias lacking temporal relation to symptoms. It is worthwhile to note that 4 of 6 such patients in this series later may have responded well to antiarrhythmic therapy. In a

previous paper from this center (11) the Adams-Stokes' syndrome was initially ruled out due to lack of correlation between arrhythmia and symptoms but a majority of these patients later improved on therapy. At the time of this study the strict criteria used in the present study were not developed. Conversely, in another series 35 out of 44 (80%) patients without therapy for significant arrhythmias had persisting cerebral symptoms (28).

There are several possible explanations for the lack of correlation between arrhythmias and symptoms in patients who really have the Adams-Stokes' syndrome. As pointed out before (13) temporary impairment of memory is part of the disorder. Failure to report symptoms (18) or the incorrect timing of events may be encountered. Other authors have reported difficulties in obtaining adequate diaries (5, 13, 20, 22), partly due to the fact that symptoms of dizziness and the like are vague and unprecise. A patient with serious arrhythmia causing major symptoms may report some minor discomfort during the recording which is then believed to have the same origin as the major complaints. Some of our patients may have lacked motivation and may have reported minor complaints in order to terminate recording.

A pertinent major reason for lack of correlation between arrhythmias and symptoms may be due to the definition of significant arrhythmias. The report of Clark et al (19) with a low incidence of patients with temporal relationships between symptoms and arrhythmia may be illustrative of this, since the same group also provided a detailed report of the application of their criteria for significant arrhythmias in an asymptomatic elderly population of 13 individuals (29). No less than 10 of these 13 subjects had significant arrhythmias. This group used a permissive classification of atrial premature contractions, to which the Lown grading system was applied, in combination with strict criteria for bradycardias - 40 bpm or less.

Patients without symptoms during the recording

Eighteen of the 19 patients with an initial 24 hour recording remained free from significant arrhythmias as LTER was extended from 24 to 48 hours. Among the 19 patients with significant arrhythmias during the initial 24 hour period 3 had an additional type of significant arrhythmia during the second period, being ventricular in all 3. Thus the originally detected types of significant arrhythmia were confirmed as the only types of significant arrhythmias in 84 per cent of those having significant arrhythmias during the initial 24 hour period.

Remarkably little is known about the increased detection of all types of significant arrhythmias attainable by prolongation of LTER. Lopes et al (23) and Jonas et al (13) reported that extension of LTER from 12 to 24 hours

resulted in considerable increases in ventricular or pertinent arrhythmias, respectively. Kennedy et al (24) found that the overwhelming majority of ventricular arrhythmias were detected within 24 hours when a comparison with additional days of recording were made. Among the entire series of 81 patients we noted that 15 of 16 cases with the sick sinus syndrome and all 4 with high degree

atrioventricular block were detected within 24 hours. However, 3 of 14 patients with atrial tachyarrhythmias required prolonged monitoring for their detection, 2 of them being observed only during symptoms.

Comparison with asymptomatic populations

In patients not experiencing symptoms during LTER the evaluation may be assisted by comparison with findings reported from asymptomatic populations.

Several investigations (30-34) have shown that almost every young, middle-aged or elderly individual will have some type of cardiac arrhythmia when ECG is extended for a sufficient period of time. A further analysis, however, discloses that sinus bradycardia is extremely common in young individuals (31, 33), while it is rare among elderly individuals (35). Although the majority of healthy subjects have some evidence of ectopic activity, the overwhelming majority of them are of an innocent nature and the percentage of subjects having complex ectopic arrhythmias is low. Furthermore, the epidemiological study of Hinkle et al (30) was later subjected to follow-ups which disclosed that both sinus bradycardia (36) and frequent or complex ventricular arrhythmia (37) had prognostic implications leaving some doubt of their normality. A recent report of patients with LTER-documented ventricular arrhythmias has demonstrated a poor prognosis (38).

Seemingly in contrast with more or less epidemiological investigations some clinically active centers have found that serious episodic arrhythmias are rare among selected normal elderly subjects (14, 35, 39). This center reported the findings made when 103 elderly individuals selected at random from the general population were examined by 24 hour LTER (26). Twenty-six of them admitted syncope and/or dizziness while 77 did not. Twelve of the 26 symptomatic and 9 of the 77 asymptomatic individuals had significant arrhythmias according to the classification currently used ($p < 0.001$). This may explain why so many of our patients had coinciding significant arrhythmia and symptoms and why, during follow-up, antiarrhythmic therapy was successful in patients who reported symptoms not coinciding with their significant arrhythmias. The use of strict criteria derived from the population study may also explain the high degree of prediction achieved from an asymptomatic 24 hour recording.

Economical aspects

The costs involved in extended recording were impressive when related to the additional information obtained. The initial or asymptomatic period revealed 40 patients with significant arrhythmias at an estimated cost of £ 130 per patient with a positive finding. The prolonged periods revealed 3 patients otherwise classified as negative and 4 instances of additional new types of significant arrhythmia at an estimated cost of £ 740 each. Facilities for LTER are limited and we prefer to screen a large group of patients with possible Adams-Stokes' attacks (40) with a 24 hour ECG rather than to prolong LTER in a small group of patients.

Conclusions

We conclude that the routine 24 hour LTER will be sufficient for detection of most patients with the Adams-Stokes' syndrome. When strictly defined criteria for significant arrhythmias are applied, the need for recording until symptoms occur will be reduced. Prolonged monitoring should be used principally in patients with problems of differential diagnostic nature or when there is a strong evidence of the Adams-Stokes' syndrome despite an initial negative recording. Provided that LTER recordings are interpreted with an open mind, the routine application of a 24 hour period should be acceptable with the understanding that prolonged monitoring may exceptionally be needed. Also when the initial LTER is negative, non-cardiogenic causes should not be ignored.

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LONG-TERM ELECTROCARDIOGRAPHIC RECORDING IN SUSPECTED ADAMS-STOKES' SYNDROME:
PART I: - DIAGNOSTIC ASPECTS

by

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Abstract

Three hundred and thirty patients with suspected Adams-Stokes' syndrome were examined by long-term electrocardiographic recording (LTER). Significant arrhythmias, i.e. arrhythmias known or presumed to correlate with cerebral symptoms, were found in 173 (52%), while only 9 (12%) of 77 asymptomatic elderly subjects had significant arrhythmias ($p < 0.001$). The fraction of patients with significant arrhythmia increased with age reaching 78% for those aged 80 years or more.

Bradycardias were found in 97 (29%) of the patients: 68 had the sick sinus syndrome (SSS) and 29 had atrioventricular block 2nd or 3rd degree (AV-bl 2^o or 3^o). Among the 76 (23%) with tachyarrhythmias 47 had ventricular arrhythmias and 29 had atrial tachyarrhythmias ≥ 120 beats per minute (bpm) and a duration > 8 seconds.

More than 80% of patients with arrhythmias previously caused by digitalis or with permanent atrial fibrillation or with heart failure had significant arrhythmias. A "fast" or "slow" pulse was frequently experienced by patients without significant arrhythmia and in patients with significant arrhythmia these complaints were frequently misleading with respect to the later finding of brady- or tachycardias, respectively.

Among patients with syncope and additional dizzy spells, 61% had significant arrhythmias compared to 35% of patients with syncope but no additional dizzy spells ($p < 0.01$). If epilepsy was previously diagnosed only 29% had significant arrhythmias. Prior strokes were almost equally common in patients with and without significant arrhythmias.

Hence various cardiac and neurological factors altered the probability of significant arrhythmia but no factor alone or in combination was associated with the absence or negligible incidence of significant arrhythmias. It is therefore concluded that all patients with symptoms suggesting the Adams-Stokes' syndrome should be entitled to long-term electrocardiographic recording.

Introduction

Disorders of cardiac rhythm have been known to cause dizziness and syncope, i.e. the Adams-Stokes' syndrome for centuries. If present only episodically these arrhythmias are likely to have an insidious character and their victims risk being interpreted as having non-cardiogenic attacks. Recently, it has become evident that the Adams-Stokes' syndrome is much more frequent than previously believed. During the last two decades several authors (1-16) have reported that as many as 26-75 per cent of patients with suspected Adams-Stokes' syndrome have serious episodic arrhythmias when examined by long-term electrocardiographic recording (LTER). Also the concept of "cardiogenic neurology", i.e. the active diagnosis and treatment of arrhythmias in patients with cerebral symptoms, has been shown to increase the local pacemaker implantation rate in a Swedish region to three times the national average (17).

The arrhythmia causing the Adams-Stokes' syndrome may be tachycardia or bradycardia and it may be iatrogenic or spontaneous. Many patients have been subjected to neurological investigations before the diagnosis of a serious episodic arrhythmia and minor arrhythmias may be detectable in the standard ECG in others.

In our department LTER has increasingly been used in the assessment of patients with syncope and/or dizzy spells. This study was performed in order to determine the frequency and distribution of serious episodic cardiac arrhythmias as detected by LTER in patients with suspected Adams-Stokes' syndrome. The cardiac and neurological symptoms and objective data were also studied and related to the detection of arrhythmias (Part I). Finally, the effectiveness of pharmacological or pacemaker treatment was assessed by means of a 3-5 year follow-up (Part II).

Material and methods

Patients

Three hundred and thirty consecutive patients referred to the Section of Cardiology for LTER due to suspected Adams-Stokes' syndrome are included in the study. One hundred and seventy-two were referred while hospitalized in the Medical Department and 148 were examined as out-patients by the author. Ambulatory patients never seen by the author are not included.

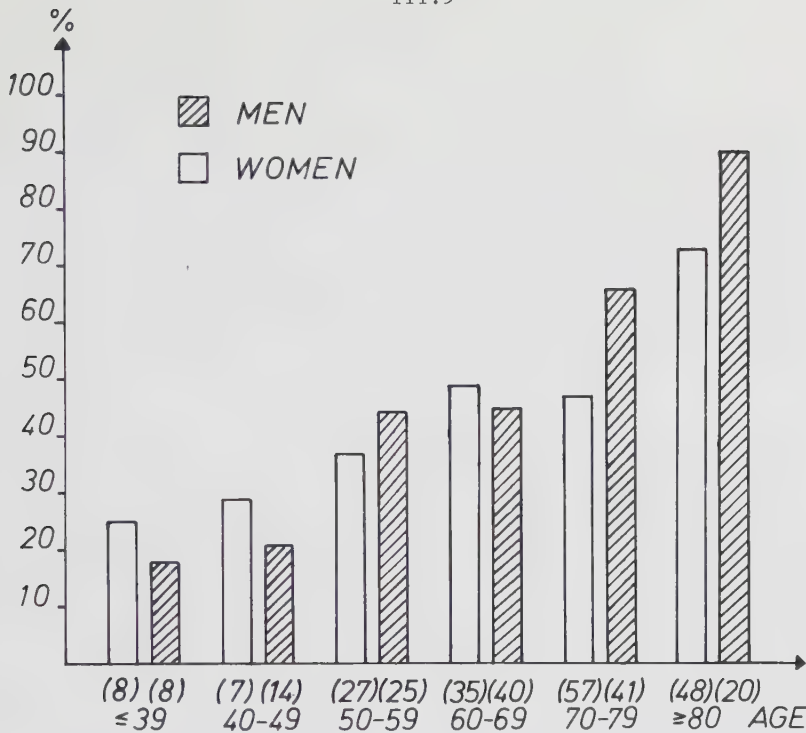


Fig. 1. Age and sex distribution and percentage of patients with significant arrhythmia in relation to age and sex. Left bar = women, right bar = men. Figures in brackets: number of patients.

Age and sex distribution of the 330 patients ($67 \pm$ S.D. 15 years) are given in figure 1. The median age was 70 years. One hundred and forty-eight were men aged 17-90 years ($65 \pm$ S.D. 15 years) and 182 were women aged 22-93 years ($69 \pm$ S.D. 15 years). A careful examination of each patient had been performed in order to detect possible non-cardiac causes of symptoms. One or more current 12-lead standard ECG was accessible for each patient.

Normal population

For each patient during the first year of the study one control individual of the same sex and day of birth was selected at random from the general population by the Population Actuary. One hundred and fifty-seven controls were invited to examination by LTER and 103 actively participated in recording for 24 hours. This study has been reported elsewhere (18). The criteria for significant arrhythmias applied in the present study are based on the findings of arrhythmias present in 26 individuals of the normal population with syncope or dizzy spells, compared to the 77 without these symptoms.

Long-term electrocardiographic recording

Using portable ECG-tape recorders type SRA/HRB-2 (Helcomed Norden/Hellige) all patients were examined until a full standard period of approximately 24 hours were obtained. In case of a technically poor recording, the examination was prolonged until a satisfactory recording covering about 24 hours was obtained. In some few uncertain cases recording was prolonged. Two hundred and sixty-three patients were examined for one 24 hour period, 15 for two 24 hour periods and 52 required prolongation to three and in some cases more days.

Screening of ECG-tapes

All ECG-tapes were analysed using an automatic unit which produced an ECG write-out when an arrhythmic event was detected. The unit was set to produce a write-out for all R-R intervals corresponding to rates ≥ 120 beats per minute (bpm) and ≤ 40 bpm, respectively. In addition, every 10th ventricular premature contraction (VPC) as detected by QRS configuration criteria within one minute of recording was presented as a write-out.

The ECG strips were then screened by specially trained laboratory technicians and by the author.

Classification of arrhythmias

The maximally occurring frequency of ectopic beats observed in a write-out was reported and graded as follows:

Infrequent: One ectopic per more than 10 regular beats,

Moderately frequent: One ectopic per 6-19 regular beats,

Frequent: One ectopic per 5 or less regular beats.

A strip containing three or more ectopic beats was used in the grading of moderately frequent or frequent ectopic beats. In addition, potentially dangerous VPCs according to Lown and Wolf (19) were reported as being of multiform origin or couplets (i.e. two VPCs in a sequence with short interval) and, when clearly occurring within the first 85% of the QT-interval of the preceeding beat, R-on-T-types. Of these only VPC-couplets will be further considered.

A tachycardia, whether atrial or ventricular, was defined as three or more beats. Nodal tachycardias were referred to atrial tachycardias (AT).

The sick sinus syndrome (SSS) was considered present when one or more of the following criteria were fulfilled: 1) Sinus brady-arrhythmia ≤ 50 bpm with a variation of consecutive P-P intervals of 20% or more, 2) Regular sinus bradycardia ≤ 45 bpm when awake, 3) Sino-atrial block, 4) Sinus arrests of $\geq 1,5$ sec.

The lowest heart rates observed during LTER were calculated from a sequence of three or more beats.

In atrial fibrillation (AF) ventricular rates of 40 bpm or less or 41-50 bpm in connection with an evident escape rhythm were referred to as atrioventricular block (AVB) 3⁰. This low rate was somewhat arbitrarily chosen to warrant symptomatic AVB, although other authors (20) consider ventricular rates of ≤ 60 bpm sufficient.

Although all arrhythmias detected were registered, this presentation is principally focused on significant arrhythmias, i.e. arrhythmias known or presumed to correlate with cerebral symptoms. Minor arrhythmias such as infrequent or moderately frequent ectopic beats are termed insignificant.

Arrhythmia diagnosis

According to the most severe or complex arrhythmia detected during LTER the patients were divided into the following groups:

No significant arrhythmia when no or only insignificant arrhythmias were detected and

Significant arrhythmias: The SSS groups contain all patients with fulfillment of the criteria required for this diagnosis irrespective of their possible additional arrhythmias. SSS-patients having additional AF or AT, i.e. the bradycardia-tachycardia syndrome, were referred to as the SSS-BTS group while those having no AF or AT were referred to as the SSS-brady group.

Atrioventricular block 2⁰ and 3⁰ were designated for patients with AVB 2⁰ or 3⁰ provided that no signs of the SSS were present but irrespective of possible additional AF/AT or ventricular arrhythmia (VA).

Frequent VPCs: This group contains all patients with frequent VPCs provided no significant bradycardia is present.

VPC-couplets/ventricular tachydardia was the designation used for patients with VPC-couplets or ventricular tachycardia (VT) provided that they have no significant bradycardia.

Atrial fibrillation/flutter or tachycardia: This group contains all patients with AF/AT ≥ 120 bpm and duration > 8 sec. not referable to the groups above.

Statistical analysis

Statistical analysis was performed using the chi-square test including Yates' correction.

ResultsMain arrhythmia diagnosis (Table I)

Table I. Main arrhythmia diagnosis in 330 patients with suspected Adams-Stokes' syndrome and in 77 controls without dizziness or syncope

Arrhythmia	Patients with suspected Adams-Stokes' (N=330)		In asymptomatic controls (N=77)		P
	N	%	N	%	
No significant arrhythmia	157	48	68	88	<0.001
Sick sinus syndrome					
Total	68	21	3	4	<0.001
Brady group	32	10	3	4	
BTS	36	11	0	0	
Atrio-ventricular block 2 ⁰ , 3 ⁰					
Total	29	9	0	0	<0.02
2 ⁰	5	2	0	0	
3 ⁰	24	7	0	0	
Ventricular arrhythmia					
Total	47	14	4	5	<0.05
Frequent VPCs	15	5	4	5	
VPC-couplets/VT	32	10	0	0	
AF/AT $\geq$ 120 bpm $>$ 8 sec.	29	9	2	3	N.S.

The number of patients referred to the respective groups of main arrhythmia diagnosis are presented in Table I, which also gives the findings made among the 77 asymptomatic elderly individuals for comparison.

No significant arrhythmia was detectable in 157 of the 330 individuals as compared with 68 of the 77 elderly subjects ($p < 0.001$).

Six of the 32 purely bradycardia SSS-patients and 7 of the 36 patients with the BTS had additional episodes of AVB 2⁰ or 3⁰. In addition, 7 and 6 patients respectively had episodes of frequent VPCs. All 3 cases of the SSS among the asymptomatic elderly individuals were of the purely bradycardic type and none of them had any additional significant arrhythmia. Five of the 29 patients with AVB 2⁰ or 3⁰ also had frequent VPCs.

For each type of significant arrhythmia other than atrial tachyarrhythmias the difference between patients and asymptomatic controls was statistically significant.

Patients with significant arrhythmia in relation to age and sex

For both men and women the percentage of patients with significant arrhythmias increased with age, being 18% among those aged 17-39 years and 78% among those aged 80 years or more. This increase with age is statistically significant (contingency table test $p < 0.001$). Within the respective decades of age there were only small and insignificant differences between men and women (Fig. 1).

Neurological symptoms
Syncope, dizzy spells and epilepsy

Table II

Table II. Number of syncopes and relation to additional dizzy spells, or dizzy spells without syncope in relation to significant arrhythmia. Previous interpretation of epilepsy in relation to significant arrhythmia.

Bradyarrhythmias: The SSS, AVB 2⁰/3⁰

Tachyarrhythmias: AF/AT, ventricular arrhythmia

	2 or more syncopal attacks		Single syn- copal attacks		No syncope but dizzy spells	Epilepsy
	n	also dizzy spells	n	also dizzy spells	n	n
No significant arrhythmia (n = 157)	72	47	17	11	68	42
Bradyarrhythmias (n = 97)	50	44	11	9	36	11
Tachyarrhythmias (n = 76)	32	26	13	10	31	6

Two or more syncopal attacks were experienced by similar proportions of patients with and without significant arrhythmia. Among patients with two or more syncope those free from additional dizzy spells were less likely to have significant arrhythmias ($p < 0.01$). Patients previously interpreted as epileptics were less likely to have significant arrhythmia ($p < 0.01$).

Other neurological symptoms (Table III)

Table III. Various neurological symptoms and diagnosis in relation to significant arrhythmia

	Cerebral athero- sclerosis	Cerebro- vascular accidents	Dependency of posture	Treatment for hypo- tension	Paroxys- mal fatigue
No significant arrhythmia (n = 157)	30	33	30	12	14
Bradyarrhythmias (n = 76)	29	24	18	13	24
Tachyarrhythmias (n = 76)	11	17	5	1	17

A previous interpretation of cerebral atherosclerosis as the cause of symptoms or a previous cerebrovascular accident with focal neurological signs was found in similar proportions of patients with and without significant arrhythmias. The same applies for dependency of posture defined as symptoms occurring predominantly in the upright position or when rising up, or previous drug treatment for hypotension. Such histories, however, suggesting posture or hypotension to be the cause of symptoms were significantly more common in patients with brady- than tachyarrhythmias ($p < 0.05$ and $p < 0.05$, respectively).

Paroxysmal unexplained fatigue was significantly more common in patients with than in patients without significant arrhythmia ($p < 0.001$).

Cardiac history in relation to significant arrhythmias
Subjective complaints (Table IV)

Table IV. Patients subjectively experiencing cardiac arrhythmia and angina or chest discomfort in relation to significant arrhythmia

Arrhythmia	"Fast"	"Irregular"	"Slow"	Angina at effort	Other angina/ chest pain
No significant arrhythmia (n = 157)	36	9	9	10	32
Brady- cardias (n = 97)	31	8	22	9	28
Tachyarr- hythmias (n = 76)	26	14	9	4	22

More patients with than patients without significant arrhythmia had experienced a "fast" cardiac action ($p < 0.05$), but there was no difference between patients with brady- and tachyarrhythmias, respectively. Even between patients with purely bradycardic SSS and the BTS there was no difference in this respect. An "irregular" cardiac action was more common in patients with than in patients without significant arrhythmia ($p < 0.05$). A "slow" pulse was more frequently observed by patients with than by patients without significant arrhythmia but several of the patients subjectively experiencing a "slow" pulse had tachyarrhythmias during LTER.

Angina at effort and angina at rest or other chest pain was only slightly more common in patients with significant arrhythmia (NS).

Objective history and findings (Table V)

Table V. Objective cardiac history in relation to significant arrhythmias. BSA: Body surface area.

	Arrhythmias presumably by digitalis	Heart failure	Cardiac enlargement $\geq 500 \text{ cc/m}^2 \text{BSA}$	Previous myocardial infarction
No significant arrhythmia (n = 157)	3	24	21	15
Bradycardias (n = 97)	18	44	53	12
Tachyarrhythmias (n = 76)	4	21	20	17

Twenty-five patients had a history of arrhythmia presumably caused by digitalis defined by the absence of arrhythmia in the standard ECG after withdrawal of digitalis. Seventeen and 6 patients had had bradyarrhythmias and VPCs, respectively during digitalis medication, while proper ECG-documentation was lacking in 2. The finding of significant arrhythmia during LTER in 22 of them was significant ($p < 0.001$).

Medication with digitalis or diuretics for heart failure or known radiological heart enlargement $\geq 500 \text{ ml/m}^2$ body surface area was more common among patients with significant arrhythmia ($p < 0.001$ and $p < 0.001$, respectively).

The increased occurrence of heart failure or known cardiac enlargement in patients with bradyarrhythmias as compared with patients with tachyarrhythmias was significant ($p < 0.05$ and $p < 0.001$, respectively). A history of definite or suspected previous myocardial infarction was somewhat more common in patients with than in patients without significant arrhythmia (NS).

Physical examination

The blood pressure was measured when lying and immediately after rising to an upright position in 119 patients without and in 121 patients with significant arrhythmia. Twenty-five and 28, respectively, had a drop in the systolic blood pressure of 15 mm of mercury or more.

Four of the 157 patients without and 5 of the 173 patients with significant arrhythmias had auscultatory valvular disease. Two of the former and 3 of the latter had aortic stenosis. Four of the five patients with valvular disease and significant arrhythmia had bradycardia.

Recent routine ECGsPermanent AF. Suggestions of bradyarrhythmia (Table VI)

Table VI. Recent ECG in relation to significant arrhythmias. Permanent AF or suggestions of bradycardia

	Permanent AF	Bradycardia ≤ 55 bpm or R-R ≥ 1.5 sec	PQ ≥ 0.22 sec	Bundle Branch Block		
				Left	Right	Bifascicular
No significant arrhythmias (n = 157)	5	6	5	9	11	3
Bradyarrhythmias (n = 97)	19	38	8	12	5	3
Tachyarrhythmias (n = 76)	5	2	3	6	3	1

The recent ECGs showed sinus rhythm in 301 patients while 29 had permanent AF. The increased prevalence of permanent AF in patients with significant arrhythmias was statistically significant ($p < 0.01$).

A bradycardia ≤ 55 bpm or an R-R-interval not being a compensatory pause ≥ 1.5 sec was associated with the finding of significant arrhythmias during LTER ($p > 0.001$), while similar proportions of patients with and without significant arrhythmia had bundle branch blocks. Furthermore, 10 of the 30 patients having bundle branch block and significant arrhythmia had tachyarrhythmias during LTER.

The routine ECGs showed sinus rhythm without any pathological changes or any additional arrhythmia in 45 of the 173 patients with and in 102 of the 157 patients without significant arrhythmia ($p < 0.001$).

Suggestions of tachyarrhythmia (Table VII)

Table VII. Ectopic activity in the recent standard ECG in relation to significant arrhythmias during LTER

LTER	APCs	Episodes of AF or AT	VPCs
No significant arrhythmias (n = 157)	8	2	9
Bradycardias (n = 97)	11	5	12
Tachycardias (n = 76)	14	2	22

APCs in the standard ECG was more frequently found in patients with than in patients without significant arrhythmia ($p < 0.01$) but a considerable proportion of the former turned out to have bradyarrhythmias during LTER. The increased tendency towards the finding of significant arrhythmias in patients with episodic AF/AT in the standard ECG was not significant. VPCs in the standard ECG was more common in patients with than in patients without significant arrhythmia ($p < 0.001$) but again a considerable fraction of the former had bradyarrhythmias during LTER.

DiscussionNumber of patients with significant arrhythmia

Using a standard period of 24 hours of applied LTER with a possibility of prolongation in technically or otherwise doubtful cases no less than 52% of the patients referred to a cardiac unit with a suspicion of Adams-Stokes' syndrome were found to have significant episodic arrhythmias. This figure is consistent with previous reports (1-16) and significantly greater than that found among elderly controls (18) ($p < 0.001$). This high proportion of patients with significant arrhythmia may be biased by the fact that all patients were referred by physicians suspecting cardiogenic causes of the cerebral attacks, but when examining an elderly population of 103 individuals selected at random, twelve of the 26 with syncope and/or dizziness had significant arrhythmias (18). This may indicate that every second individual of old age with syncope and/or dizziness may suffer from significant episodic arrhythmia detectable within 24 hours of LTER regardless of the occurrence of symptoms during the recording. The fraction of patients with significant arrhythmias increased significantly with age (Fig. 1) but nevertheless every fifth patient with syncope and/or dizziness below the age of 40 years had significant arrhythmia. This indicates

that LTER may successfully be applied even in younger patients.

Previous LTERs in healthy subjects

In the past there has been some doubt cast on the clinical relevance of episodic arrhythmias since several studies have shown that virtually everyone has some kind of arrhythmia when LTER is applied. Sinus arrhythmia or bradycardia is very common in young adults according to Engel and Burckhardt (21) and Brodsky et al (22) but Camm et al (23) found that it is a less frequent phenomenon in healthy elderly subjects. Thus the criteria for sinus node dysfunction should preferably be correlated to age.

In middle-aged or aged populations epidemiological studies have shown that ectopic activity is very common. Among men in their mid-50s Hinkle et al (24) found that the majority of them had atrial or ventricular ectopic activity, while only 2% had sino-atrial or high degree atrioventricular block. Clarke et al (25) and Adey et al (26) made similar findings. Hinkle (27) and Hinkle et al (28) later showed that both ventricular ectopy and sinus bradycardia had prognostic implications. Seemingly in contrast with these epidemiological findings investigators also publishing clinical studies tend to find that the fraction of healthy elderly subjects with serious arrhythmias is low (13, 18, 23, 29). One exception is the normal population presented by Glasser et al (30) who examined only 13 asymptomatic elderly subjects and had a permissive definition of significant atrial ectopic arrhythmia combined with strict criteria for bradycardia. This offers a possible explanation for their failure to demonstrate differences in ectopic arrhythmias between their healthy elderly subjects and their symptomatic elderly patients (31).

Types of significant episodic arrhythmias

In suspected Adams-Stokes' syndrome a wide spectrum of various episodic significant arrhythmias was detectable by LTER. In the present study, patients with bradycardia were somewhat more common than those with tachyarrhythmia. Furthermore, the SSS was twice as common as AVB 2⁰ or 3⁰.

The high proportion of patients with the SSS as compared with AVB 2⁰ or 3⁰ has also been found by other investigators using LTER (4, 7, 8, 14, 15). However, when determining the epidemiology of bradycardias as detectable by the routine ECG a similar incidence for the SSS and AVB 2⁰ and 3⁰ was found during the last sampling years of the study by Shaw and Kekwick (32), but still only about 25% of all pacemakers implanted in the western hemisphere are on account of the SSS (33, 34). A possible explanation for the dominance of the SSS in bradycardias detected by LTER could be patients selection due to a more insidious and episodic character of the SSS. It is also noteworthy that 18 of the present 24

patients classified as AVB 3⁰ had permanent atrial fibrillation, 12 of them with bradycardia ≤ 55 bpm in the routine ECG.

Another explanation for the dominance of SSS in episodic bradycardias could be the use of permissive criteria. Our criteria, however, followed the concepts of Ferrer (35) and the rate requirements were based on findings made in an elderly population selected at random (18). Then 6 of 26 individuals with and 3 of 77 without syncope and/or dizzy spells had the SSS according to the criteria currently used. It might be added that the 3 asymptomatic subjects with the SSS had severe sinus bradycardia or sino-atrial block leaving no doubt of sinus node dysfunction. The recent report of Camm et al (23) with the finding of only 4 cases of sinus bradycardia of 50 bpm or less when awake in 98 elderly individuals confirms the accuracy of the currently used criteria for the SSS as diagnosed by LTER.

Although we noted that a main arrhythmia diagnosis of a tachycardia was less common than one of a bradycardia, others (2, 3, 4, 6, 14, 15, 31) have found more patients with tachycardias than bradycardias. The reason for this discrepancy among published series is not fully understood but differences in diagnostic criteria and LTER equipment, clinical settings and referral patterns may be explanatory.

Ventricular arrhythmias were detected in 47 of the 330 patients and there is little doubt that such patients suffer from significant arrhythmia. The inclusion of patients with atrial tachyarrhythmias > 8 sec may be questioned as the fraction of patients with these arrhythmias was not significantly greater than that in the normal population. However, episodic AF and AT can produce cerebral symptoms as proven by a temporal relationship with symptoms (3, 36). Furthermore, dramatic hemodynamic changes during atrial tachycardias were demonstrated by Goldreyer et al (37) in patients reporting a temporal relationship between arrhythmia and cerebral symptoms.

Neurological history and significant arrhythmia

A history of syncopal attacks without dizzy spells was less frequently presented by patients with than by patients without significant arrhythmia. Although there was a significant difference ($p \leq 0.01$) it must be kept in mind that a considerable proportion of patients with syncope but no dizzy spells had significant arrhythmias. Also patients with significant arrhythmia were less prone than patients without significant arrhythmia to have a previous diagnosis of epilepsy. Again, despite a significant difference ($p \leq 0.001$) a considerable proportion of patients with a previous interpretation of epilepsy turned out to have significant arrhythmia. This is consistent with the report of Schott et al (38) of arrhythmias that masquerade as epilepsy and the finding (17, 39) that

many pacemaker treated patients had an earlier diagnosis of epilepsy.

Thirteen per cent of patients with significant arrhythmia experienced symptoms only in the upright position. Obviously, many patients with the Adams-Stokes' syndrome require orthostatism + arrhythmia before hemodynamic effects are manifested. In patients with episodic significant arrhythmia and a history suggesting orthostatic hypotension the arrhythmia risks going undetected. On the other hand, patients extensively followed due to impending AVB may turn out to have hypotension but no arrhythmia when carefully assessed following cerebral symptoms (40, 41).

Paroxysmal severe fatigue was an outstanding complaint in 24% of patients with but only 9% of patients without significant arrhythmia. It might be appropriate to incorporate this complaint into the list of symptoms associated with the Adams-Stokes' syndrome.

Neurological examinations and significant arrhythmia

A history of prior stroke with focal neurological signs had no predictive implication. This may be due to a marked risk of cerebral embolization among patients with the SSS (42, 43, 44) or chronic AF without valvular disease (45). Even patients with episodic AF or AT without concomitant signs of the SSS may possibly be at risk but investigations covering this subject have not been published (46).

The possibility of cardiac arrhythmia producing both general cerebral ischemic episodes and cerebral embolization should be kept in mind. Hence a prior stroke is no definite indication that syncopal attacks or dizzy spells are of primarily cerebral origin.

Cardiac history and significant arrhythmia

Cardiac complaints were of little value in the differentiation between patients with and without significant arrhythmias. Angina and chest pain and subjectively experienced arrhythmia were equally common in patients with and without significant arrhythmias. Furthermore, every fourth patient with a subjective history of "fast" rhythms turned out to have bradycardias and frequently patients with a "slow" pulse had tachyarrhythmias. This lack of correlation between palpitations of LTER-documented arrhythmias was recently stressed by Kunz et al (47) and Zeldis et al (16) who monitored their patients until symptoms. It is evident that treatment for the Adams-Stokes' syndrome should not be based on the patient's subjective complaints of arrhythmia. Monitoring of the cardiac rhythm is needed to establish the true nature of any possible arrhythmia before therapy for the Adams-Stokes' syndrome is commenced.

Objective cardiac findings and significant arrhythmias

Objective cardiac data provided the best prediction of significant arrhythmia. A previous documentation of arrhythmia caused by digitalis or treatment for cardiac failure was strongly associated with the finding of significant arrhythmia.

Atrial fibrillation, a noted bradycardia or ectopic beats in the standard ECG increased the probability of significant arrhythmia during LTER. However, various types of bundle branch blocks were not associated with an increased incidence of bradycardias among this series of patients with suspected Adams-Stokes' syndrome. It is also remarkable that 10 of the 30 patients with bundle branch blocks and significant arrhythmia had tachyarrhythmia during LTER, a finding supported by others (40, 48).

Despite the association between significant arrhythmias and findings in the recent standard ECG many patients had completely normal standard ECGs. Again, the clinical history suggesting Adams-Stokes' syndrome may be the most reliable and simple indication of possible serious episodic arrhythmia.

Conclusions

In patients with symptoms in agreement with the Adams-Stokes' syndrome the majority was found to have significant arrhythmia on LTER. Various other cardiac or neurological symptoms increased or decreased the probability of significant arrhythmia, but no single factor was capable of excluding it with reasonable accuracy. It is therefore concluded that all patients with clinical symptoms suggesting the Adams-Stokes' syndrome should be entitled to LTER.

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LONG-TERM ELECTROCARDIOGRAPHIC RECORDING IN SUSPECTED ADAMS-STOKES' SYNDROME:
PART II - FOUR YEAR FOLLOW-UP

by

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Abstract

Three hundred and thirty patients referred to a cardiac unit with suspected Adams-Stokes' syndrome were examined by long-term electrocardiographic recording for 24 hours or more. One hundred and seventy-three of them who had significant episodic arrhythmias were followed for 3-5 years.

Fifty-three of 65 patients with brady-arrhythmias and 56 of 62 patients with tachy-arrhythmias responded to adequate therapy with the improvement of symptoms. In contrast, symptoms persisted in 22 of 30 patients with brady-arrhythmias and in 13 of 14 patients with tachy-arrhythmias who were not given adequate therapy. Spontaneous recovery was observed in 8 (26%) patients not adequately treated for bradycardias but in only one (7%) patient not treated for tachy-arrhythmia.

Despite the excellent response to therapy, 35 of the 173 patients were admitted to permanent geriatric hospitalization. The risk of subsequent need for permanent geriatric hospitalization was unrelated to the electrocardiographic severity of the arrhythmia or the intensity of therapy. However, 31 of the 126 patients with atrial arrhythmias associated with systemic embolization were admitted to permanent geriatric hospitalization as compared to 4 of 47 patients without such atrial arrhythmias. This difference is significant and suggests that the risk of permanent disability is related to both atrial arrhythmias and the hemodynamics of the arrhythmia. The importance of systemic embolization was further emphasized by the finding of possible non-cerebral arterial embolizations in 21 patients and encephalomalacias in 28 patients.

These data demonstrate that therapy for significant arrhythmias causing Adams-Stokes' syndrome should always be attempted. The majority of patients respond to therapy with improvement of symptoms; however, the long-term risk of permanent disability possibly caused by systemic embolization constitutes a constant threat. Future studies are needed, however, to determine whether the inclusion of prophylactic treatment against embolization in patients with atrial dysfunction will reduce the later need for permanent geriatric hospitalization in patients with the Adams-Stokes' syndrome.

Introduction

Long-term electrocardiographic recording (LTER) is well documented as an efficient tool in the diagnosis of occult episodic arrhythmias believed to cause the Adams-Stokes' syndrome (1-16). According to previous reports, the overwhelming majority of such patients show an excellent short-term response to therapy with the abolishment of cerebral symptoms, but, in a few, symptoms persist, suggesting another origin. Johansson (11) extended follow-up to two years, but further long-term reports are lacking.

Diagnosis and subsequent therapy of serious episodic cardiac arrhythmias causing cerebral symptoms may, however, have long-term implications other than the abolishment of the Adams-Stokes' syndrome. Survival, morbidity patterns and long-term need for permanent geriatric hospitalization may be influenced.

Part I of this series reported the diagnostic aspects of 330 patients referred to a cardiac unit due to suspected Adams-Stokes' syndrome. By means of LTER for 24 hours or more, 173 (52%) were found to have significant arrhythmias, i.e. arrhythmias known or presumed to correlate with cerebral symptoms. The objective of this report - part II - is to assess: 1) The long-term response of arrhythmias to therapy resulting in the improvement of cerebral symptoms, 2) The survival of such patients in relation to various therapies, 3) The mode of death and 4) The long-term need for permanent geriatric hospitalization.

Patients and methods

Patients

The patient material has been presented in detail in Part I. In summary, this material comprised 330 patients aged 17-93 years (mean 67 ± 15 years). One hundred and forty-eight were men, aged 17-90 years (mean 65 ± 15 years), and 182 were women, aged 22-93 years (mean 69 ± 15 years). All patients were referred to the Section of Cardiology because of suspected Adams-Stokes' syndrome. Syncope had been experienced by 195 patients and 135 had suffered from dizzy spells.

Long-term electrocardiographic recording

Using portable ECG-recorders type SRA/HRB-2 (Helcomed Norden/Hellige) all patients were monitored for approximately 24 hours. In 77 patients the recordings were prolonged due to poor quality or - in a few cases - due to borderline findings.

Screening of ECG-tapes

The ECG-tapes were screened by an automatic unit which produced ECG-write-outs when an arrhythmia was detected. Single R-R-intervals corresponding to rates of 120 beats per minute (bpm) or more and 40 bpm or less triggered a write-out, as did every 10th ventricular premature contraction (VPC) according to configuration criteria and occurring within one minute.

Classification of arrhythmias

This presentation is principally limited to patients with significant arrhythmias, i.e. arrhythmias known or presumed to correlate with cerebral symptoms. Other arrhythmias were termed insignificant and are omitted. Classification of significant arrhythmias was based on the findings made in an elderly population selected at random and monitored for 24 hours by LTER (17). Significant arrhythmias were:

Frequent VPCs , i.e. one VPC per 5 or less beats in a sequence containing three or more VPCs. In addition, potentially dangerous VPCs according to Lown and Wolf (18) were recorded but of these only VPC-couplets are considered here.

Ventricular tachycardia (VT), i.e. three or more consecutive VPCs.

The sick sinus syndrome (SSS) was diagnosed when one or more of the following criteria were fulfilled: 1) Sinus-brady-arrhythmia ≤ 50 bpm with a variation in consecutive P-P-intervals of 20% or more, 2) Regular sinus bradycardia ≤ 45 bpm when awake, 3) Sino-atrial block, and 4) Sinus arrests ≥ 1.5 sec. The lowest heart rates were calculated from a sequence of three or more beats. All patients with the SSS were referred to this group irrespective of additional possible arrhythmias. Patients with the SSS and additional episodes of atrial tachy-arrhythmias were designated as having the bradycardia-tachycardia syndrome (BTS).

Atrial fibrillation (AF) or atrial tachycardia (AT) including nodal forms were considered significant provided a ventricular rate ≥ 120 bpm and a duration > 8 sec.

Atrio-ventricular block (AVB) 2⁰ and 3⁰. In patients with permanent AF, AVB 3⁰ was considered present if the ventricular rate was 40 bpm or less, or 41-50 bpm in connection with an evident escape rhythm as measured from 3 consecutive beats.

Statistical method

The chi-square test including Yates' correction was used for statistical analysis.

Follow-up

Patients with significant arrhythmia were followed as out-patients. Follow-up averaging 4 years was compiled chiefly by retrospective review of patient files. Patients who failed to attend as out-patients or had moved from Malmö were interviewed by phone or assessed by review of patient files from other hospitals etc. None was lost to follow-up. Survival was checked at the Population Actuary and all death certificates and autopsy reports, when existing, were obtained.

Survival rates

For groups of patients, the expected survival rate of an age- and sexmatched Swedish population was calculated using the life table method. Death risks were obtained from the Statistical Abstracts of Sweden (19).

ResultsMain arrhythmia diagnoses (Table I)

Table I. Main arrhythmia diagnosis in 173 patients with significant arrhythmia. VPC = ventricular premature contraction, VT = ventricular tachycardia

BradyarrhythmiasSick sinus syndrome

Bradycardia only	32
Bradycardia-tachycardia syndrome	36

Atrio-ventricular block

Second degree	5
Third degree	24

Tachyarrhythmias

<u>Atrial tachy-arrhythmia</u>	29
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Ventricular arrhythmia

Frequent VPCs	15
VPC-couplets/VT	32

Of the 330 patients, 173 with significant arrhythmias were classified according to their main arrhythmia diagnosis (Table I). Of the 68 patients with the SSS, 13 also had episodes of AVB 2^o or 3^o. Among the 15 patients with a main arrhythmia diagnosis of frequent VPCs, 2 had R-on-T-types and one had VPCs of multifocal origin.

Therapy for the Adams-Stokes' syndrome

Therapy for arrhythmia was given when considered appropriate by the attending physician. Accordingly, the patients could be divided into two groups - those receiving and those not receiving active treatment.

Patients who continued to have syncopal episodes or stated that their dizzy spells were unchanged were classified as having persisting symptoms. Patients without further syncopal attacks who stated that they had no further dizzy spells or a substantial reduction in the frequency and severity of dizzy spells were classified as improved. Evaluation of symptoms after LTER was undertaken by the author. This assessment was based upon the patient's subjective complaints according to patient files which also contained information regarding any acute conditions causing visits to the Emergency Room or hospitalization in the Medical Department.

Bradycardias (SSS, AVB 2⁰/3⁰) actively treated (Table II)

Table II. Treatment of bradycardias in relation to improved or persisting symptoms.

Active therapy	Symptoms		Mean Follow-up (months)
	Improved	Persisting	
Digitalis omitted or reduced	16	4	52
Atropine, sympathicomimetics	6	1	53
Pacing	23	4	59
Miscellaneous	8	3	47
	53	12	
No active therapy or disregarded			
Pacing recommended but not performed	1	6	55
No therapy	7	13	48
Digitalized	0	3	51
	8	22	
Not evaluated: 2			

Digitalis omitted or reduced and not paced: In 20 patients digitalis was either discontinued (15) or reduced (5). Five patients had the brady-SSS, 2 had the BTS, and 13 had AVB 2⁰ or 3⁰. Symptoms improved in 16 but persisted in 4. In 14 patients, LTER was repeated with the finding of the disappearance or reduction of the bradycardias.

Atropine and sympathicomimetics: Two patients with the SSS received atropine but only one of them improved. Four patients with the SSS and one with AVB 3⁰ were given sympathicomimetics, all with improvement of symptoms.

Pacemaker treatment: Twenty-seven patients were paced, including 4 patients with continued bradycardia despite digitalis withdrawal. Twenty-three of the 27 paced patients reported improved symptoms, but in 5 of these additional anti-arrhythmic treatment for tachy-arrhythmias was also given.

Miscellaneous: Six patients with the BTS and only mild bradycardias but troublesome tachycardias were given anti-arrhythmic preparations. Symptoms improved in 4 of them. Two of 3 patients with the SSS experienced improvement when beta-blockers triggering bradycardias were withdrawn. One patient with the SSS recovered from both bradycardia and cerebral symptoms following potassium substitution for hypokalemia, and one patient with a moderate sinus bradycardia improved after being given dihydroergotamine for orthostatic hypotension.

Bradycardias not actively treated or disregarded

Pacemaker therapy recommended but not performed: In 7 patients pacemaker therapy was recommended but not initiated. In 6 of these, symptoms persisted but one patient improved spontaneously. Two additional patients expired shortly after LTER.

No therapy: Twenty patients with brady-arrhythmias received no treatment. Sixteen had the BTS and 4 had permanent AF and atrio-ventricular block 3⁰. In 13 symptoms persisted and in 7 there was spontaneous improvement.

Digitalized: In 3 patients with the SSS the arrhythmia was disregarded and digitalis given for concomitant heart failure. All deteriorated.

Not evaluated

Two patients with recommendation of cardiac pacing were not evaluated as they expired before any meaningful assessment could be made.

Summary of treatment versus non-treatment in bradycardias

Of the 65 patients actively treated for bradycardias, 53 were evaluated to have shown improvement, while 12 had persisting symptoms. Of the 30 who were not treated or who were disregarded, the corresponding figures are 8 and 22, respectively.

The lowest heart rates during LTER were 35.9 ± 7.5 bpm (mean $\pm$ SD) among patients actively treated as compared with 39.4 ± 6.9 bpm (mean $\pm$ SD) in patients not actively treated.

Tachy-arrhythmias actively treated (Table III)

Table III. Treatment of tachy-arrhythmias in relation to cerebral symptoms.

Active therapy and type of arrhythmia	Symptoms		Mean Follow-up (months)
	Improved	Persisting	
Atrial tachy-arrhythmias	21	3	51
Frequent VPCs	11	1	50
Coupled VPCs/ Ventricular tachycardia	24	2	52
	56	6	
No active therapy			
Type of arrhythmia			
Atrial tachy-arrhythmias	1	4	51
Frequent VPCs	0	3	49
Coupled VPCs/ Ventricular tachycardia	0	6	50
	1	13	

Atrial tachy-arrhythmias: Twenty-four patients were actively treated for AF or AT. Digitalis-induced arrhythmias were diagnosed in 5 who had no further tachycardias or cerebral symptoms following digitalis withdrawal. On the other hand, digitalis was given to 7 patients, 6 of whom experienced improvement in symptoms. Two patients were given quinidine and two were given verapamil, all 4 experienced improvement. Beta-blockers were used in 8, 6 of whom improved.

Frequent VPCs: Withdrawal of digitalis was effective in 3 patients who then showed improvement of cerebral symptoms. Seven patients were given anti-arrhythmic preparations, 6 showing improvement of cerebral symptoms. Two patients with moderate alcohol over-consumption demonstrated improvement of both arrhythmia and cerebral symptoms following reduction of their alcohol intake.

VPC-couplets/ventricular tachycardia: Two patients showed improved cerebral symptoms following digitalis withdrawal. Twenty-two patients, including 3 in whom digitalis withdrawal was initially performed without success, received anti-arrhythmic drugs. After the initial treatment with a single anti-arrhythmic drug, LTER was repeated in 17. The simultaneous use of two or more anti-arrhythmic preparations was then required in 4 of them. Twenty-one of the 22 patients who received anti-arrhythmic drugs showed improvement of cerebral symptoms.

One patient had no further arrhythmia after discontinuation of levodopa, although his cerebral symptoms persisted. One patient used terbutaline inhalation spray for bronchial asthma and symptoms ceased after discontinuation of the drug.

Tachy-arrhythmias not actively treated

Four of 5 patients with atrial tachy-arrhythmias and all 9 with ventricular arrhythmias who received no treatment remained symptomatic.

Summary of treatment versus non-treatment in tachy-arrhythmias

Fifty-six of 62 patients actively treated showed improvement of cerebral symptoms; 6 did not. Only one of 14 patients who were given no treatment improved spontaneously.

Four-year-survival

Bradycardias actively treated: In 47 patients treated by cardiac pacing or reduction or withdrawal of digitalis, the four-year-survival rate was 60% as compared with an expectation of 69%. There was a small difference between patients paced and patients treated by digitalis reduction or withdrawal, 57% and 64%, respectively.

Bradycardias not actively treated: Among patients who were not treated in any way for their bradycardias, the four-year survival was 48% as compared with an expected rate of 67%.

Tachy-arrhythmias actively treated: The four-year-survival rate of patients actively treated for AF/AT was 65% as compared to an expected rate of 78%. No deaths occurred in patients who were given beta-blockers or in patients who had their digitalis discontinued.

One of the 12 patients treated for frequent VPCs died.

The overall four-year survival rate for the 26 patients treated for VPC-couplets or ventricular tachycardia was 47% as compared to an expected rate of 76%. However, these patients may be divided into two groups: One consisting of 17 patients who were re-monitored by LTER following the principles of Lown and Graboys (20), until effective therapy which abolished all potentially dangerous VPCs was found; the other group consisting of 9 patients, all 60 years of age or more, who were simply given anti-arrhythmic treatment until subjective complaints disappeared. All 8 patients below the age of 60 years with therapeutic monitoring survived. Five of the 9 patients 60 years or older with therapeutic monitoring survived, as compared to none of the 9 who were only symptomatically treated.

Tachy-arrhythmias not treated: Only two of the 5 patients with AF/AT not actively treated survived. All three patients with frequent VPCs not treated survived, while 5 of the 6 patients not treated for VPC-couplets/ventricular tachycardia died within 14 months after LTER.

Long-term geriatric hospitalization

(Table IV)

Table IV. Various arrhythmia groups with and without active treatment in relation to long-term geriatric hospitalization.

	With atrio-pathic arrhythmia		Without atrio- pathic arrhythmia	
	Total	In long-term geriatric hos- pitalization	Total	In long- term ger- iatric hospi- tali- zation
Bradycardias treated				
Digitalis omitted or reduced	17	6	3	0
Paced	23	9	4	0
Other	17	2	1	0
Bradycardias not treated				
All incl. digitalized	30	7	2	0
Tachy-arrhythmias treated				
Atrial tachy-arrhythmias	24	1		
Frequent VPCs	0	0	12	0
VPC-couplets-ventricular tachycardia	9	3	17	4
Tachy-arrhythmias not treated				
Atrial tachy-arrhythmias	5	2		
Frequent VPCs	0	0	3	0
VPC-couplets/ventricular tachycardia	1	1	5	0

Table IV shows the various arrhythmia groups according to type of treatment in relation to long-term geriatric hospitalization during follow-up. Each group of patients was divided into two subgroups: One with atriopathic arrhythmias, defined as permanent or episodic AF, AT or SSS, and one group without atriopathic arrhythmia. The latter group was composed principally of patients with normal sinus rhythm plus episodes of either atrio-ventricular block 2^o or 3^o or ventricular arrhythmia.

Among the 126 patients having some form of atriopathic arrhythmia, 31 had been treated on a permanent basis in geriatric hospitals during follow-up as compared to 4 of the 47 without atriopathic arrhythmia. Nineteen of the 31 patients with atriopathic arrhythmias and admissions to permanent geriatric hospitalization had suffered a clinically known stroke.

Patients with bradycardias had greater need for later geriatric hospitalization than patients with tachy-arrhythmias, 24 of 97 versus 11 of 76 ($p < 0.01$). It is also evident from Table IV that vigorous and effective treatment for bradycardias did not result in a reduced need for later geriatric hospitalization: 15 of the 47 patients treated by pacing or digitalis withdrawal or reduction later required permanent geriatric hospitalization as compared to 9 of the 50 less vigorously treated (N.S.).

Deaths and autopsy findings
Immediate cause of death

(Table V)

Table V. Immediate cause of death in patients with significant episodic arrhythmia.

Sudden	6
Stroke	13
Acute myocardial infarction	12
Heart failure	3
Pulmonary embolism	10
Pneumonia	12
Non-cerebral arterial embolization	5
Malignancy	3
Miscellaneous	6

Table V is a summary of the immediate causes of death in the 70 patients who expired during follow-up. The figures are based on autopsy findings in 63 instances and clinical diagnoses in 7.

Six patients suffered sudden death, defined as instant death without explanation at autopsy. Two of these were unpaced despite recommendations, while 3 patients with the SSS died suddenly shortly after digitalization for atrial fibrillation. One patient with episodic AI died suddenly without any suggestive circumstances.

Place of death. Nine patients died outside the hospital. Thirty-three died in the General Hospital following acute illness, while 28 died in geriatric hospitals after a long downhill course.

Autopsy findings. Recent and previous myocardial infarctions were found in 25 patients and 20 others had advanced coronary atherosclerosis, i.e. 45 of 63 patients had evidence of coronary heart disease at autopsy. It is noteworthy that all types of arrhythmia were associated equally with coronary disease. Five patients had cardiac amyloidosis.

Encephalomalacias were detected in 28 patients, 11 of whom had no, or only minimal cerebral atherosclerosis. Signs of non-cerebral arterial embolizations were found in 21 patients. Sixteen patients had probable splenic or renal infarctions in addition to the 5 in whom these were the direct cause of death.

Discussion

The management of patients with the Adams-Stokes' syndrome has the following primary objectives: To reduce symptoms of syncope and/or dizziness, to reduce the risk of death and to reduce the risk of cerebral damage and its associated need for permanent institutional care.

Improvement of symptoms of syncope and/or dizzy spells

The overwhelming majority of patients experienced abolishment or definite improvement of syncope and/or dizziness following adequate therapy. Eighty-two per cent and 90% of patients treated for brady-arrhythmias and tachy-arrhythmias, respectively, responded well to therapy. Among patients not treated, however, only 27% and 7%, respectively, had spontaneous improvement of their symptoms. These results may possibly indicate that tachy-arrhythmias are more closely related to cerebral symptoms or that the chance of spontaneous recovery is greater in brady-arrhythmias but further studies are needed to confirm or reject either of these hypotheses. It is noteworthy, however, that only 12% of 282 patients paced due to bradycardia had spontaneous (normal) rhythm at all check-ups during follow-up of an average of almost six years (21).

The rate of successful control of symptoms was similar to that reported by others (3, 6, 11, 13) and the therapeutic failures may have several explanations. Dizzy spells are experienced by every fifth individual aged 75 years or more (22). Obviously, some patients may have both significant arrhythmia and dizziness or even syncope caused by other mechanisms. Despite this, the simple classification of arrhythmias as significant and subsequent initiation of appropriate therapy proved clinically useful in 86% of the patients to whom this procedure was applied.

Permanent geriatric hospitalization - role of atrio-pathic arrhythmias

Despite improvement in their symptoms of syncope and dizziness, 35 patients were admitted to permanent geriatric hospitalization during this follow-up averaging four years. This institutionalization was equally common among patients who might be regarded as adequately treated as among patients not subject to therapy for their arrhythmias (Table IV). Therefore, a factor other than the hemodynamic severity and frequency of occurrence of arrhythmias must be responsible for the increased need for permanent geriatric hospitalization.

Permanent atrial fibrillation is well known to carry an increased risk of systemic cerebral embolization (23, 24). The sick sinus syndrome, as well, carries with it an increased risk of cerebral embolism, both when paced and not paced (25, 26). In the Malmö series of episodic SSS, the annual risk of cerebral embolization was estimated to be 7% per patient (27). Episodic atrio-pathic arrhythmia was recently found to be a common cause of stroke (28). Among the total of 126 patients having such atrio-pathic arrhythmias, 31 were admitted to permanent geriatric hospitalization as compared to 4 out of 47 patients having no atrio-pathic arrhythmia ($p < 0.05$). It may therefore be suspected that atrio-pathic arrhythmias and the concurrent risk of possible cerebral embolization are major causes of long-term severe disability in patients with the Adams-Stokes' syndrome.

In patients with atrio-pathic arrhythmias and Adams-Stokes' syndrome, thus, the treatment of the arrhythmias per se is rewarding and offers excellent relief from troublesome symptoms of generalized cerebral ischemic episodes. Nevertheless, sooner or later, a considerable proportion of them end up in permanent geriatric hospitalization. From a humanitarian standpoint this is disappointing. Future studies are needed to determine if the inclusion of the atrio-pathic concept with prophylactic treatment for systemic embolization will improve the long-term quality of life.

Survival

Generally, the excess mortality was moderate and attributable to underlying cardiac disease, but some points may be of interest. Patients adequately treated for bradycardia had a four year survival rate close to the expected rate. Similar experiences from cardiac pacing have been reported by others (29). However, patients with no or inadequate treatment of bradycardias had a reduced four-year-survival rate, but this increased mortality may be explained by sudden deaths occurring in patients with bradycardias who were either digitalized or not paced despite recommendations. The prognosis for patients with unpaced permanent AVB 3⁰ as documented by the routine ECG is disastrous (30), but the prognosis of patients with unpaced episodic AVB 3⁰ is unknown. The annual mortality in a large series of patients with unpaced episodic SSS, however, was about 10%, and, since additional episodes of AVB 2⁰ or 3⁰ had an insignificant influence on survival, the natural history of episodic AVB 2⁰ or 3⁰ may be more benign than hitherto anticipated(31). It is noteworthy that all five sudden deaths in patients with bradycardia may in retrospect have been clinically avoidable.

Patients with malignant ventricular arrhythmias who were not therapeutically monitored following the principles of Lown and Graboyes (20) had the worst outcome. With use of the LTER for therapeutic monitoring, however, survival was fairly good. The LTER deserves recognition not only as a tool to diagnose these patients, but also for the testing of optimal therapy.

Deaths and autopsy findings

Despite the capacity of serious episodic arrhythmias to cause alarming symptoms, sudden and presumably arrhythmic deaths were few. Among 146 un-paced patients it occurred in 6. Fifteen of the remaining 64 deaths were due to clinically recognized cardiac disease. A maximum of 18 additional deaths may have been due to cardiac disorder with possible systemic embolization. Hence the majority of deaths was due to proven or suspected cardiac disease.

Forty-five of the 63 patients subjected to autopsy had signs of coronary atherosclerosis or myocardial infarction.. This is, however, not an indication that the majority of deaths in patients with significant arrhythmias have underlying ischemic heart disease, since they represent only the fraction of patients who expired during a four-year follow-up.

Encephalomalacias were found in 28 of the 63 patients with undergoing post-mortem examination, 11 in patients with no or only minimal cerebral atherosclerosis. Furthermore, no less than 21 had signs of possible non-cerebral arterial embolizations. The occurrence of strokes in patients without cerebral atherosclerosis and the high number of non-cerebral embolizations are further

indications of the importance of systemic embolization in patients with episodic arrhythmias.

Conclusions

Therapy for significant arrhythmias in patients with suspected Adams-Stokes' syndrome is rewarding despite the lack of a demonstrated temporal relationship between arrhythmia and symptoms. Since the overwhelming majority of such patients responds to correction of arrhythmias with an improvement of symptoms, therapy should always be attempted when clinically indicated. Episodic cardiac arrhythmias are treatable causes of symptoms and the chance of spontaneous recovery is small.

Therapy should be primarily aimed at alleviation of symptoms. The risk of sudden death is less than previously believed, but possible systemic embolization seems to constitute a major threat to the long-term quality of life. Future studies are needed to assess whether prophylactic treatment for embolization will reduce the burden of episodic significant arrhythmia.

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Unrecognized intermittent bradycardias in patients treated for senile dementia

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During the last decade pacemaker implantation rates have steadily increased in different countries (Hori et al., 1973; Karlöf and Lagergren, 1973; Sykosch, 1973; Verhey, 1973). It has been reported that increased facilities for cardiac monitoring in a Swedish region resulted in a pacemaker implantation rate 3 times the national average (Abdon and Malmcrona, 1973a, b). The exact demand for pacemakers in a population is still undetermined. Reports indicate that patients with transient cerebral ischemia frequently suffer from dysrhythmia (Walter et al., 1970) and that they are easily misinterpreted (McAllen and Marshall, 1973). Epilepsy may be the first diagnosis (Edhag, 1969). Thus our hypothesis was that patients treated for senile dementia might suffer from unrecognized intermittent arrhythmias.

Material and methods

All 63 patients in two wards of a psycho-geriatric hospital, treating exclusively patients with senile dementia, were studied. The wards were considered to have the most physically disabled dementia patients in the hospital. They were with few exceptions referred from our own hospital. Figure 1 shows patient age and sex. Deaths in each age group are also given (follow-up was 30 months).

According to Swedish law, a statement by a physician that a patient suffers from advanced psychiatric disease making him legally incapacitated is necessary upon commit-

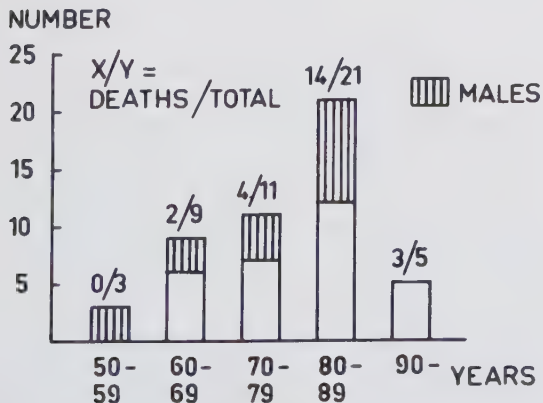


Fig. 1 Age and sex of the patients.

TABLE 1

Significant intermittent arrhythmias in 32 patients with post-apoplectic dementia

Second or third degree AV block	6
Second or third degree AV block with episodes of ventricular tachycardia	2
Sinoatrial block	1
Sick sinus syndrome	2
Supraventricular tachycardia	6
Ventricular bigeminy or trigeminy	2
Ventricular tachycardia	1

TABLE 2

Arrhythmias in 17 patients with terminal dementia

Sinoatrial block	1
Sinus bradycardia	1
Supraventricular tachycardia	3
Ventricular bigeminy	1

ment. All patients were classified as having dementia by a psychiatrist. Using an ECG-recorder type SRA, the ECG was recorded on every patient for 24 hours. In case of an unsuccessful recording one more attempt was made. Patient agitation and technical difficulties reduced the number of acceptable recordings to 35 covering 24 hours, and 14 covering at least 12 hours.

The tapes were screened by an automatic unit. All pulse rates faster than 120 or slower than 40 beats per minute as well as every 10th ventricular ectopic beat were presented as a one lead ECG on a paper strip (sensing on R-R intervals). All doubtful records were omitted. Minor arrhythmias such as isolated ectopic beats were excluded from this study. Technical difficulties made detailed diagnosis doubtful in some cases but the method seemed quite reliable with regard to beat-to-beat intervals.

The patients were divided into 2 groups: (1) 32 patients with no previous psychiatric hospital treatment before the current admission, largely classified as "atherosclerotic" or "post-apoplectic" dementia; (2) 17 patients with chronic psychiatric disorders such as alcoholism or schizophrenia and in the stage of so-called terminal dementia.

Results

Arrhythmias in the post-apoplectic group (Table 1): 8 patients had second or third degree atrioventricular (AV) block, 2 of them in combination with episodes of ventricular tachycardia. Sinoatrial block was found in 1 patient and 2 patients had the sick sinus syndrome. Supraventricular tachycardia was present in 6 patients. Ventricular bigeminy or trigeminy was found in 2 patients and 1 had episodes of ventricular tachycardia.

Arrhythmias in the terminal dementia group (Table 2): Sinus bradycardia at a rate of 25 beats per minute and sinus arrest was found in 1 patient. Her routine ECG showed a sinus rhythm at a rate of 45 beats per minute which had been considered harmless. She had had diphtheria during adolescence and after this developed mental retardation and an 'intractable epilepsy'. Sinoatrial block was found in one patient and 3 patients had supraventricular tachycardia. Ventricular bigeminy was present in one patient.

Clinical cardiac disease (Table 3): 10 of the 23 patients without serious intermittent arrhythmias had had no previous myocardial infarction, heart failure or significant arrhythmia according to their hospital records. The corresponding figure was 14 among the 26 patients with intermittent arrhythmia.

Neglected previous arrhythmia or suggestive routine ECG (Table 4): In the post-apoplectic group 2 patients had a history of third degree AV block during digitalis medication. The drug had been omitted and a cardiac origin of their later syncopal attacks had

not been suspected. This study revealed an intermittent third degree AV block in both patients. Another patient had a previously unsuspected right bundle branch block and left anterior hemiblock and was found to have intermittent third degree AV block. One patient was thought to have mild sinoatrial block which was found to be of serious character, while one patient with atrial tachycardia and sinus arrhythmia and one patient with atrial flutter were found to have the sick sinus syndrome.

Fractures (Table 5): Of the 23 patients without arrhythmias, 2 had fractured a femoral neck and 2 had other fractures or were X-rayed on suspicion. Among the 26 patients with arrhythmias, 11 had fractured a femoral neck — 5 of them in combination with other fractures. Other fractures or suspected fractures were present in 5 patients.

Neurological attacks (Table 6): Due to the physical disability it was in most instances impossible to find out whether a patient had actual syncopal attacks or not. In the group without arrhythmias 1 patient had a diagnosis of epilepsy and 4 had experienced cerebrovascular accidents. In the arrhythmic group 4 patients had epilepsy and 10 an earlier cerebrovascular accident (without focal neurological signs).

TABLE 3

Previous cardiac disease

In 23 patients with normal long term ECG	
Myocardial infarction	2
Heart failure	9
Serious arrhythmia	3
No previous cardiac diagnosis	10
In 26 patients with intermittent arrhythmia	
Myocardial infarction	1
Heart failure	9
Serious arrhythmia	5
RBBB + LAH	1
No previous cardiac diagnosis	14

TABLE 4

Neglected previous arrhythmias or ECG and corresponding monitored ECGs in patients with post-apoplectic dementia

Neglected arrhythmia or previous ECG	Monitored ECG
2 cases of third degree AV block during dig- italis medication	Intermittent third degree AV block despite digitalis having been stopped
1 case of RBBB+LAH	Intermittent third degree AV block
1 case of sinoatrial block	Sinoatrial block
1 case of atrial flutter	Sick sinus syndrome
1 case of atrial tachycardia and sinus arrhythmia	Sick sinus syndrome

Deaths

All patients have been followed for 30 months. Of the 23 patients without arrhythmias, 8 have died. Among 26 patients with arrhythmias, 16 have died. The average time between admission and death was 4 years among patients with arrhythmias. A post mortem examination was carried out on every patient except one. The pathologists were not informed about this study and the causes of death are listed below (as given by the pathologists).

TABLE 5

Fractures in relation to arrhythmias

In 23 patients with normal monitored ECG	
Fracture of the femoral neck	2
Other fractures or X-ray on suspicion	4
In 26 patients with intermittent arrhythmia	
Fracture of the femoral neck	6
Fracture of the femoral neck and one or more other fractures	5
Other fractures or X-ray on suspicion	5

TABLE 6

Hospital treatment for neurological attacks in relation to arrhythmia

In 23 patients with normal monitored ECG	
Epilepsy	1
Cerebrovascular accident	4
In 26 patients with intermittent arrhythmias	
Epilepsy	4
Cerebrovascular accident	10

Deaths in patients without arrhythmia

The causes of death were bronchopneumonia (4), pulmonary embolus (1), myocardial infarction (1), pulmonary edema following a myocardial infarction (1) and metastatic carcinoma of the kidney (1). The hearts and brains of 7 patients were examined. Coronary atherosclerosis or myocardial infarction was present in all of them. The severity of cerebral atherosclerotic disease was moderate only in one case, but the other patients had advanced atherosclerosis of the cerebral vessels.

Deaths in patients with intermittent arrhythmia

Atrial bradycardia: 4 of 5 patients in this group died. Both patients with sinoatrial block died of heart failure following acute cholecystitis. One patient with the sick sinus syndrome died from myocardial infarction and one patient with sinus bradycardia had an esophageal rupture. Myocardial fibrosis was found in both patients with sinoatrial block and all patients with atrial bradycardia had coronary disease, their cerebral vessels being virtually unaffected.

Supraventricular tachycardia: 2 of 9 patients in this group died, both from bronchopneumonia. Post-mortem examination showed one had minimal coronary atherosclerosis and the other myocardial infarction. Both had advanced cerebral atherosclerosis which in one case was combined with a finding of senile plaques.

AV block: 7 of 8 patients in this group died. The causes of death were bronchopneumonia (3), bronchopneumonia and glomerulonephritis (1), bronchopneumonia and pulmonary edema (1), heart failure following acute cholecystitis (1) and mesenteric thrombosis (1). Statements were made on 5 hearts — all had coronary atherosclerosis and 4 of them had myocardial fibrosis. Advanced cerebral atherosclerosis was found in 5 of the 6 brains examined.

Ventricular arrhythmia: 3 of the 4 patients in this group died. The causes of death were esophageal rupture (1) and bronchopneumonia (2). Coronary atherosclerosis was present in all patients in this group. Two patients had cerebral atherosclerosis. The patient with ventricular tachycardia had multiple areas of cerebral softening without atherosclerotic vessels.

Discussion

A considerable proportion of patients treated for post-apoplectic dementia were found to have serious intermittent arrhythmias. A later study among physically healthy demented patients in nursing homes having no history consistent with Adams-Stokes attacks has shown virtually no arrhythmia (Abdon, to be published). Eleven of 32 patients with post-apoplectic dementia had bradycardias. A history of possible Adams-Stokes attacks was obtainable in 9 of them. Although 6 were treated with digitalis a neglected earlier need for cardiac pacing cannot be excluded. Since most arrhythmia patients at autopsy also had advanced cerebral atherosclerosis, the long term benefit of a pacemaker must be questioned. However in the group with supraventricular bradycardia no cerebral atherosclerosis was found and the possible benefit of a pacemaker seems greater.

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Discussion

DR. MALMCRONA: Could it in fact be said that quite an important etiology of senile dementia has now been discovered. You said that there was only an implication for pacemaker treatment. But are there other therapeutic implications from this work?

DR. ABDON: I think that this is not the etiology of senile dementia, but I think that some patients might be considered to have senile dementia, if they have a hidden bradycardia.

DR. JOHANSSON: If the arrhythmia was an important contributing factor to these symptoms, it would be possible to divide these patients into different groups. Was it possible from the clinical history to separate those with arrhythmias from those without?

DR. ABDON: Yes, it was, because if a patient had a history of repeated fractures, and hospital treatment for neurological attacks such as epilepsy or suspected strokes, you could be almost certain that you would find arrhythmias among them.

Episodic Cardiac Arrhythmia and Femoral Neck Fracture

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ABSTRACT. Fifty-eight consecutive patients admitted to hospital for fracture of the upper end of the femur were examined by continuous ECG monitoring for 22–24 hours. More than one third of the patients had occult, previously unknown episodic arrhythmias severe enough to cause dizzy spells and syncope. These patients had more often a history of dizziness and syncope and could less frequently than patients without serious arrhythmias return to their homes at the time of discharge despite uncomplicated fracture treatment.

Key words: arrhythmia, ECG, fracture, femoral neck.

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Episodic cardiac arrhythmias may cause dizziness and fainting. In patients with such symptoms, serious episodic arrhythmias have been found by continuous ECG monitoring in incidences ranging from 20 to 74% (2, 5, 6, 7, 8, 11). Increased risk of trauma is common in patients with episodic arrhythmia causing dizziness and syncope. In a series of patients with Adams-Stokes syndrome treated with pacing, no less than 13% had been admitted to hospital because of trauma prior to pacemaker implantation (3). This liability disappeared during pacemaker treatment. Transient cardiac arrhythmia is an elusive condition which may not be recognized for a long time or ever.

Femoral neck fracture—fracture of the upper end of the femur—is related to aging (4) and impaired quality of the bone and is regarded as one of the typical symptoms of bone fragility (9). However, it is generally agreed that a trauma in most instances is needed to cause a fracture, even if the trauma in itself would not cause injury to a subject with an intact bone quality.

The two conditions—fracture of the neck of the femur and occult cardiac arrhythmia—are both common in an aging population. The purpose of the present investigation was to study the possible role

of occult arrhythmias in patients with femoral neck fracture.

PATIENTS AND METHODS

Included in the study were 58 consecutive patients aged 51–91 (77 ± 11), 12 men (aged 73 ± 11) and 46 women (aged 78 ± 11), admitted to the Orthopedic Department. Twenty-six of the fractures were trochanteric and 32 cervical. None of the patients had local bone destructions or other findings indicating a pathological fracture, one woman had a somewhat dubious impacted cervical fracture. The fractures were eventually treated with reduction and osteosynthesis, but were in all managed in traction for at least 24 hours of preoperative preparations. On admission, a detailed cardiac and neurological history was recorded in each case. A radiogram of the heart and lungs was performed in all patients in connection with the diagnosis of fracture.

Preoperatively, a continuous ECG monitoring covering 22–24 hours was performed using portable ECG tape recorders, type SRA/HRB-2 (Helcomed Norden/Hellige). There was no change in the cardiac medication until the ECG recording was completed except for a few patients who received diuretics due to congestive heart failure. The ECG tapes were stored and analyzed after discharge using an automatic screening unit. Rhythms faster than 120 or slower than 40 beats/minute detected by single beat-to-beat interval triggered the screening unit to present the event as a written one-channel ECG on a paper strip. In addition, every 10th premature ventricular contraction (PVC) detected by QRS configuration criteria was presented. The further diagnostic procedure included a screening by specially trained laboratory technicians and finally by one of us (N.-J. A.).

All signs of arrhythmia were recorded. Minor arrhythmias of types normally occurring in healthy subjects have been referred to as insignificant. Major arrhythmias with an inherent capacity of causing cerebral symptoms were considered significant. Such significant episodic arrhythmias were: Abundant PVCs—i.e. every 5th beat or more frequently—coupled PVCs and ventricular tachycardias defined as three consecutive PVCs at a rate of at least 100 beats/min, atrial tachycardias including fibrillation and flutter providing a ventricular rate of 120 beats/min or more and a duration of more than 8 sec, atrioventricular

Abbreviations: PVC=premature ventricular contraction, PAC = premature atrial contraction, SSS = sick sinus syndrome.

blocks of grades 2 or 3 and finally the sick sinus syndrome (SSS) fulfilling one or more of the following criteria: 1) Sinus bradyarrhythmias of 50 beats/min or less. 2) Regular sinus bradycardia of 45 beats/min or less when awake. 3) Sinoatrial block with more than one P-wave missing. 4) Sinus arrests of 1.5 sec or more.

In addition to the monitored ECG, serial 12-lead routine ECGs were recorded and serial S-GOT and S-GPT determinations were made for three consecutive days after admission. This procedure revealed no case of definite or suspected acute cardiac disorder.

In addition to the detailed questionnaire used on admission, the record room of the Medical Department was searched for information on earlier complaints of dizzy spells and syncope as well as cardiac symptoms in the fracture patients. The record room of the Roentgen Department was also searched for information on trauma episodes for the last five years preceding the femoral neck fracture. The City of Malmö is served by one single hospital—the General Hospital—and the emergency room of the Medical Department is the only unit available for emergency consultations regarding neurological or cardiac symptoms. Thus, it is assumed that the overwhelming majority of such patients are registered in the record room of the department. Practically all trauma roentgen is also carried out in the General Hospital.

The fracture patients were compared with 103 individuals, randomly selected from the population at risk, 53 men and 50 women with an average age of 71 years (range 47–92) who had been studied with regard to arrhythmias using the very same method of 22-hour continuous ECG monitoring. Out of these individuals, 26 had complaints of dizzy spells whereas 77 denied all forms of dizziness or syncope.

RESULTS

Patients with insignificant arrhythmias only

In 35 patients, aged 75 ± 11 , no or only insignificant episodic arrhythmias were detected. One had chronic atrial fibrillation with an appropriate ventricular rate, 34 were in sinus rhythm. Fourteen patients had infrequent (i.e. less than every 10th beat) premature atrial contractions (PACs) and 8 had abundant or moderately frequent PACs (i.e. at least one PAC in 5 and 6–10 beats, respectively). Two patients had short bursts of atrial tachycardias lasting for 8 sec or less. Eighteen patients had infrequent or moderately frequent PVCs.

Patients with significant episodic arrhythmias

In 23 patients, aged 79 ± 10 , significant episodic arrhythmias were detected (Table I). Six patients had episodes of atrial tachycardias including fibrillation lasting longer than 8 sec with ventricular rates of 120 beats/min or more. Nine patients had abundant

Table I. *Episodic arrhythmias in 77 asymptomatic controls and 58 patients with fracture of the upper end of the femur*

	Asymptomatic controls		Fracture cases	
	N	%	N	%
SSS	3	4	2	3
Attacks of rapid supra-ventricular rhythms	2	3	6	10
High-frequency PVCs, ventricular bigeminy	4	5	9	14
Ventricular tachycardia			3	5
Atrioventricular block, grade 2 or 3	9	12	3	5
			23	40

$p < 0.001$ (χ^2 -test).

PVCs or ventricular bigeminy and three had ventricular tachycardias. Episodes of sinus bradycardia fulfilling the criteria used for SSS were present in two patients and transient atrioventricular block of grade 2 or 3 was present in three patients.

Mortality and discharge from hospital

Five of the 23 patients with significant arrhythmia and four of 35 without died during hospitalization. This doubled mortality was, however, not statistically significant. Despite uncomplicated fracture healing, only 4 of the 18 surviving patients with significant arrhythmias had a general physical condition permitting return to their homes after discharge, whereas 15 of the 31 survivors without significant arrhythmias could return to their homes without permanent or transient need for institutional care. Again, the difference was not significant. There were no signs of acute cardiac disease in any of the 58 patients—the subsequent departure in 9 of the cases was in most instances due to pulmonary embolism.

The ratio cervical/trochanteric fractures was 19/16 in the group without and 13/10 in the group with significant arrhythmias.

Previous dizziness and significant arrhythmia

Fifteen out of the 23 patients with and 12 out of the 35 patients without significant episodic arrhythmias had visited the Department of Medicine because of dizziness and/or syncope or had reported this type of symptoms on admission for fracture ($p < 0.05$).

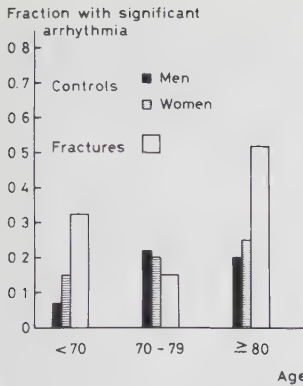


Fig. 1. Incidence of significant arrhythmia in fracture cases compared with all "normals", symptomatic as well as asymptomatic.

The admission chest X-ray showed cardiac enlargement in 5/23 of the arrhythmic cases and in 10/35 of those without significant arrhythmia. There was no significant difference in this aspect. However, resting ECG showed definite previous myocardial infarction, ischemic T-wave inversions or arrhythmia in 7/23 arrhythmic patients and in 1/35 patients without significant arrhythmia. This difference is statistically significant ($0.01 > p > 0.001$).

There was no difference in the frequencies of earlier trauma episodes between fracture patients with and without significant arrhythmia.

Comparison with normals

Significant arrhythmia was approximately three times as common in femoral neck fracture cases as in the asymptomatic controls (Table I). The arrhythmias in the fracture group were also more serious and long-lasting than in the asymptomatic normals. However, it must be taken into account that the age and sex distribution of the two groups was different. The 26 symptomatic "normals" who demonstrated significant arrhythmia in 12 cases could also be included in the comparison. The age and sex incidence of symptomatic arrhythmia is presented in Fig. 1, including all 103 normals. The incidence shows a tendency to increase with increasing age but does not differ significantly between the sexes. When comparing the femoral neck fracture cases with the normals, taking the age into account, there is still a significant difference in the

prevalence of arrhythmia among the youngest and the oldest in the two groups.

DISCUSSION

As pointed out above, serious episodic arrhythmias have been demonstrated in a high incidence in patients with dizziness and syncope. However, only few asymptomatic individuals, even of advanced age, have serious episodic arrhythmias (2, 10). The findings of the present study indicate a significant increase in serious episodic arrhythmias, a possible contributory cause of fracture. This view is supported by the findings in 32 patients, 20 of whom had episodic arrhythmias, treated for "post-apoplectic" dementia in a psycho-geriatric hospital in the City of Malmö. Not less than 11 had also sustained a fracture of the upper end of the femur (1). Among 23 demented patients in the same hospital but without episodic arrhythmia, only 2 had had femoral neck fracture.

Fracture of the neck of the femur is a stressful condition, possibly capable of triggering arrhythmia. Arrhythmia then would be a result rather than a cause of the trauma. However, patients with significant arrhythmias had more often a history of dizziness than those without. Furthermore, since patients with significant arrhythmia had a markedly increased need of institutional care following the fracture episode, it might be argued that even if the trauma has triggered off the arrhythmia in some cases, this tendency might nevertheless be inherent with the patient and, regardlessly, resulting in a poor prognosis.

The mortality among our 58 fracture patients was about 15% which is in agreement with the mortality figure in a previous study of the same population (4). Although the difference between the two groups is not significant, both the mortality and the ability of the patient to sustain without institutional care after discharge from hospital indicate a worse post-fracture course for femoral neck fracture patients with serious arrhythmia even if the age factor must be taken into consideration. The most serious prospect for these patients is probably the increased risk of continuing impairment of the cerebral function. The method of continuous ECG monitoring has proven its value in the diagnosis of occult episodic cardiac arrhythmia and will probably be a routine diagnostic tool in the future. Patients with fracture of the upper end of the femur appear to be a worthwhile target for such diagnostic efforts.

N.-J. Abdon and B. E. Nilsson

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IS OCCULT ATRIAL DISEASE A FREQUENT CAUSE OF NON-HEMORRHAGIC STROKE? -
LONG-TERM ECG IN 86 PATIENTS

By

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Introduction

Atrial disorder may cause stroke by two potential mechanisms: by arrhythmias causing decreased cardiac output, i.e. hemodynamic stroke, or by left atrial thrombus formation with subsequent systemic embolization. There is little evidence that sudden hemodynamic changes are of clinical importance. Brain infarcts are rare among survivors of cardiac arrest (1) and although focal neurological signs may be observed in connection with cardiac arrhythmias (2,3) only few patients paced for bradycardia have such a history (4). On the other hand, atrial fibrillation with or without mitral valve disease causes cerebral embolization from left atrial thrombus formation (5-8). In the Framingham study the risk for developing stroke showed an almost six-fold increase after the onset of atrial fibrillation in ischemic heart disease (9). Recently prolapse of the mitral valve has been associated with stroke in young patients (10) and with atrial arrhythmias (11).

Patients manifesting atrial disease by having the sick sinus syndrome (SSS) have also been found to develop cerebral embolization, both when paced and not paced (12-14). During a 4.5 year period 254 new cases of mainly episodic and mild SSS were diagnosed in Malmö (15). These diagnoses were obtained by long-term electrocardiographic recording (LTER) of patients with suspected Adams-Stokes' syndrome. They had a subsequent annual incidence of cerebral emboliza-

tion of 7.2% (16). The risk for cerebral embolization was unrelated to the severity and duration of bradycardias but patients having the bradycardia-tachycardia syndrom (BTS), i.e. SSS with additional episodes of atrial fibrillation (AF) or atrial tachycardia (AT), had nearly twice the risk of patients having purely bradycardic SSS.

Thus atrial fibrillation, atrial tachycardia, and the SSS may - whether permanent or episodic - be regarded as a common group of "atriopathic arrhythmias" (APA) predisposing for atrial thrombus formation and systemic embolization. Among 103 elderly controls selected at random and subjected to 24 hour LTER no fewer than 23 had atripathic arrhythmias (17) consistent with possible risk for embolization. These arrhythmias reflecting atrial disease may well be a frequent cause of non-hemorrhagic stroke.

In this study we investigate the prevalence of such atripathic arrhythmias by means of LTER in a consecutive series of patients with non-hemorrhagic stroke.

Patients and methods

Patient sampling and classification of strokes

This study includes all patients having acute non-hemorrhagic stroke with focal neurological signs consecutively admitted to three wards of the Medical Department of the General Hospital in Malmö during a five month period. The cardiac intensive care ward was not included thereby excluding most cases of acute myocardial infarction of obvious threatening arrhythmias. As one of the wards almost exclusively admits men there is a male overrepresentation.

All patients and/or their relatives were subjected to a standardized interview on arrival to the wards. A detailed cardiac and neurological history was obtained and a physical examination was performed. A special protocol was used and later evaluated by the senior staff physician. Using these data all strokes were classified mainly according to the principles of Millikan et al. (18) and were given the following designations:

Transient ischemic attacks (TIA) in cases of two or more completely reversible attacks of short duration and never exceeding 24 hours with the same neurological signs or symptoms; Embolization in cases where a neurological defect developed within seconds and was not preceded by prodromal signs, irrespective of past or present cardiac arrhythmia; Thrombosis in cases with a gradual onset of neurological signs or having prodromal signs. The thrombotic group also includes all cases with an unknown mode of onset including those developing stroke during sleep. Patients with a diagnosis of intracranial hemorrhage were not included.

Lumbar punctures, brain scans, ECGs and angiographic studies were performed according to the clinical situation. Computerized tomography was not available for routine use at the time of the study.

LTER and classification of arrhythmias

On days 2-6 after arrival the patients were examined by LTER for approximately 24 hours using portable ECG tape recorders type SRA/HRB-3 (Helcomed Norden/Hellige). This period of monitoring was chosen since the prolongation of LTER up to 48 hours in patients with suspected Adams-Stokes syndrome only increased the fraction of patients having atriopathic arrhythmia by 4% (Abdon, unpublished data). In order to avoid bias all tapes were coded and tapes from ward patients with suspected Adams-Stokes syndrome and patients free from cardiac and neurological signs were also coded and analyzed. No information regarding age, sex, or clinical data was available to the ECT interpreter.

All ECG-tapes were analyzed using a semi-automatic processing as described elsewhere (17). Heart rates were calculated from three or more cardiac cycles and given as beats per minute (bpm). Ventricular premature contractions (VPCs) were classified according to their maximal occurrence detected at any time during the 24 hour LTER. Only patients with frequent VPCs (i.e. one VPC per five or less beats) are included in the results. In addition, potentially dangerous VPCs (19) (i.e. multifocal VPCs, "couplets" = two in a sequence with short interval and R-on-apex-T types) were noted.

In cases with the fulfillment of one or more of the following criteria:

1) Sinus bradyarrhythmia with a difference in consecutive sinus cycles of 20% or more ≤ 50 bpm, 2) regular sinus bradycardia ≤ 45 bpm when awake, 3) sino-atrial block and 4) sinus arrests ≥ 1.5 seconds the designation sick sinus syndrome was given irrespective of drug effects. Patients with the SSS and episodes of AF or AT were considered to have the bradycardia-tachycardia syndrome.

The LTERs from stroke patients were compared with those from a reference group of 103 elderly individuals randomly selected from the population of Malmö and described in a previous report (17). They had been examined using the same equipment and classification as in the present study. Nine of the 103 individuals had a probable history of stroke.

Statistical analysis

Statistical analysis was performed using the chi-square test including Yates' correction. Data were cast in 2x2 contingency tables and the null hypothesis of independence of row and column variables was tested.

Results

TIAs were diagnosed in 18 patients, 14 men and 4 women aged 51-85 years (mean $68 \pm$ s.d. 8 years). Two of them had the SSS, both with a moderate sinus bradycardia induced by betablockers. Three TIA-patients had permanent AF and one had paroxysmal AT. Thus 6 (33%) of the TIA patients had atripathic arrhythmia.

Cerebral thrombosis was diagnosed in 33 patients, 20 men and 13 women, aged 51-88 years (mean 74 ± 10). In 8 of these patients an SSS was found, being of the BTS type in 4. Six patients had permanent and one had paroxysmal AF. Thus 15 (45%) of the patients with cerebral thrombosis had atripathic arrhythmia.

Cerebral embolization was diagnosed in 35 patients, 26 men and 9 women, aged 48-89 years (mean 69 ± 10). During LTER 11 had the SSS which was of the BTS type in 8. Permanent AF was present in 3 patients and 3 had paroxysmal AF/AT. Accordingly atripathic arrhythmias were found in 17 (49%) of the patients with cerebral embolism.

Previous strokes and atriopathic arrhythmia

Table 1. Previous strokes in other vascular areas and atriopathic arrhythmia (APA) in patients with TIA and thrombotic or embolic stroke

Type of stroke	Previous stroke		No previous stroke	
	Number	APA	Number	APA
TIA	3	1	15	5
Thrombotic or embolic	16	13	52	19

Among the 18 TIA-patients 3 had suffered a previous stroke from another focus. One of them had the SSS. Among the 15 remaining TIA-patients 5 had atriopathic arrhythmia. Among the 68 patients with cerebral embolization or thrombosis 52 had no previous stroke in other vascular regions. Nineteen of these 52 had atriopathic arrhythmias as compared to 13 of the 16 patients with previous strokes in other vascular areas. In cerebral embolism and thrombosis this difference in atriopathic arrhythmias between patients with and without stroke in other areas is significant ($p < 0.05$).

Evidence of prior atriopathic arrhythmia

The SSS was found during LTER in a total of 21 patients, 8 of them having ECG-tracings recorded prior to the stroke showing atriopathic arrhythmias. Seven of the 17 patients with AF or AT had previous ECG documentation of the arrhythmia.

Standard admission ECG

The standard admission ECG showed atriopathic arrhythmia in 17 (20%) as compared with the 38 (44%) having it during LTER.

Table 2. Current or previous history or documentation of atriopathic arrhythmia in patients with thrombotic or embolic stroke. APA = atriopathic arrhythmia.

	History of APA	No history of APA
Current APA	23	9
No current APA	12	24

In addition to prior ECG documentation a history of dizziness or palpitation may suggest an atrio-pathic arrhythmia being present prior to the stroke. Such definite or suggestive evidence of prior atrio-pathic arrhythmia was present in 23 of the 32 patients with embolic or thrombotic stroke who had atrio-pathic arrhythmia during LTER. In the remaining 36 embolic or thrombotic patients without atrio-pathic arrhythmia during LTER 12 had previous ECG documentation or histories consistent with pre-existing atrio-pathic arrhythmia. This difference is significant ($p < 0.01$). It is noteworthy that the latter group includes 3 patients who had severe sinus bradycardia during earlier digitalis medication.

Non-cerebral systemic embolization

In 3 patients with the SSS, verified retinal artery embolization with monocular blindness had occurred and one patient with AF had suffered an embolization of the femoral artery. Only one patient without atrio-pathic arrhythmia had experienced non-cerebral arterial embolization and it had occurred in connection with an acute myocardial infarction.

Hypertension. Previous myocardial infarction

Patients with a systolic blood pressure ≥ 175 or a diastolic ≥ 115 mmHg or receiving anti-hypertensive treatment were classified as hypertensive. Among the 35 patients with hypertension 17 had atrio-pathic arrhythmia as compared with 21 of the 51 non-hypertensive patients. Twenty patients had had a previous myocardial infarction. Nine of them had atrio-pathic arrhythmias as opposed to 29 of the 66 patients without previous myocardial infarction. Neither difference was significant ($p > 0.05$).

Arrhythmias in relation to clinical outcome

According to the clinical outcome the patients were divided into two groups: 24 patients with complete recovery and 62 who had no or incomplete recovery or death ($n = 7$). Twenty-one of all patients with sequelae required permanent institutional care following the stroke. After recovery from the initial TIA 10 of the 18 TIA-patients developed new symptoms during hospitalization. Six of these had minimal sequelae and 4 developed completing stroke.

Table 3. Clinical outcome in stroke patients with atriopathic arrhythmia and/or hemodynamically important arrhythmias.

AV-b = atrio-ventricular block

VA = frequent VPCs or potentially dangerous VPCs

Type of arrhythmia	Death or residual symptoms (n = 62)	Complete recovery (n = 24)
SSS - no additional arrhythmia	6	3
SSS + AV-b 2 or 3 ⁰ and/or VA	11	1
AF/AT - no additional arrhythmia	7	1
AF/AT + AV-b 2 or 3 ⁰ and/or VA	9	0
AV-b 2 or 3 ⁰ , no atriopathic arrhythmia	0	1
VA - no atriopathic arrhythmia	3	3

Thirty-three (53%) of the 62 (mean age 71 ± 9 years) who did not have complete recovery had atriopathic arrhythmias as opposed to 5 (21%) of the 24 (mean age 69 ± 11 years) who recovered completely. This difference is significant ($p < 0.01$).

Additional hemodynamically important arrhythmias were common in patients with a poor clinical outcome and atriopathic arrhythmia. Among the 33 patients with atriopathic arrhythmia who expired or had sequelae 20 had additional atrio-ventricular block 2⁰-3⁰ or frequent or potentially dangerous VPCs. An isolated atrio-ventricular block 3⁰ was detected in one patient with complete recovery who returned to normal sinus rhythm during LTER after discontinuation of digitalis. It is also noteworthy that 5 of the 6 patients with isolated hemodynamically important ventricular arrhythmia were TIA-patients with ischemic heart disease, 4 of them having appropriate atheromatous lesions at aorto-cervical angiography.

Aorto-cervical angiograms

Aorto-cervical angiograms were performed in 28 patients considered for possible endarterectomy. Twelve had TIAs and in 16 a first TIA could not be excluded. Twenty of the 28 patients had atheromatous lesions corresponding to the neurological deficit. In 17 of these 20 patients there were no atriopathic arrhyth-

mias while one had the SSS and 2 had AF/AT. Two of the remaining 8 patients had severe atheromatous lesions not corresponding to the site of the neurological lesion, both without atriopathic arrhythmias. Finally, 6 patients had essentially normal vessels with the finding of atriopathic arrhythmia in 3 of them.

Table 4. Correlation of roentgenologic findings with neurological symptoms and arrhythmia in the 28 patients studied with angiography.

* Atheromatous plaque corresponding to localization of the current neurological symptoms. APA = atriopathic arrhythmia.

Arrhythmia	Appropriate lesion*	Other lesion	No lesion
No APA	17	2	3
SSS	1	0	1
AF/AT	2	0	2

Carotid artery surgery was uneventfully performed in 15 of the patients with appropriately located lesions. All were found to have ulcerated plaques at surgery.

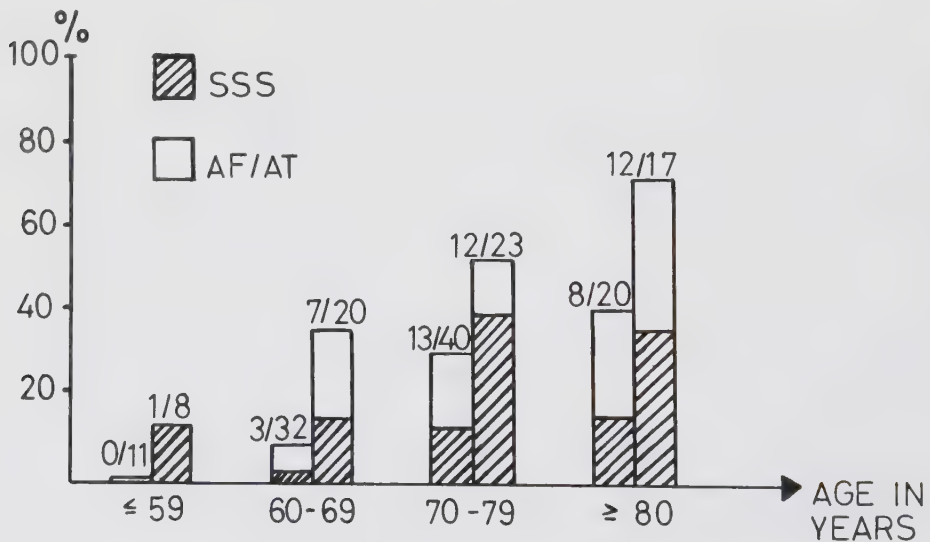


Fig. 1. Prevalence of atrio-pathic arrhythmias in the reference population (left bar) and patients with thrombotic or embolic strokes (right bar) in relation to age.

Figure 1 gives the age related prevalence for men and women together of atriopathic arrhythmias in patients with embolic or thrombotic stroke for comparison with the 103 elderly controls selected at random and subjected to LTER during a previous study (17). Within the respective age brackets the prevalence of atriopathic arrhythmias was always increased among patients with embolic or thrombotic stroke as compared with the controls. Beginning with a 13% prevalence in stroke patients 59 years of age or younger there was a steady increase to as much as 71% for those aged 80 years or more. The corresponding increase in atriopathic arrhythmias in controls was from 0 to 40%.

Table 5. Prevalence of atriopathic arrhythmia detected by LTER in control and stroke populations.

* Only thrombotic or embolic strokes are included.

Age	M E N		W O M E N	
	Controls	Stroke*	Controls	Stroke*
≤60 years	2/26	5/24	1/17	3/4
≥70 years	9/27	11/22	11/33	13/18

This table illustrates the same control and stroke populations with respect to atriopathic arrhythmia, sex and age. For statistical analyses some age groups have been pooled. The groups of male and female stroke patients differed significantly (chi square 9.91, d.f. 3, $p < 0.025$), the age-related prevalence being uniformly higher among females. For the statistical comparison of control and stroke populations, data for males and females were summed in the respective age classes. Control and stroke populations were clearly different (chi square 10.14, d.f. 3, $p < 0.025$). In each age group the combined male and female prevalence of atriopathic arrhythmia of stroke patients exceeded that of controls. There were proportionately more males in the stroke than in the control population. As even female stroke patients had a higher prevalence of atriopathic arrhythmia the relatively high prevalence of arrhythmia in the stroke population seems to be related to stroke itself rather than to differences in the age and sex distributions among controls and patients.

Discussion

In the present study three main observations associating atrio-pathic arrhythmia with non-hemorrhagic stroke were made:

- 1) The prevalence of atrio-pathic arrhythmias among patients with non-hemorrhagic stroke was 44%, being twice that found in the control population. This difference is significant and not explained by differences in age and sex distribution between controls and patients. The number of patients with AF/AT is higher than or agrees with the results of other investigators (20-24). In addition, we find a large number of patients with the SSS, possibly due to the sensitivity of the diagnostic technique.
- 2) ECG-documentation of previous atrio-pathic arrhythmia was available in 15 of the 38 patients with atrio-pathic arrhythmias during LTER. A history of dizziness or palpitation indicating possible previous atrio-pathic arrhythmia was found in 8 additional patients. Thus 3/5 of patients with atrio-pathic arrhythmia during LTER had definite or possible previous atrio-pathic arrhythmia.
- 3) A history of multiple neurological foci suggesting systemic embolization was present in 16 cases, 13 of which had atrio-pathic arrhythmia during LTER. Furthermore, 4 of 5 patients with non-cerebral arterial embolization had atrio-pathic arrhythmias, the fifth as previously mentioned being in connection with acute myocardial infarction. Conversely, when the current neurological lesion could be explained by an angiographically demonstrable lesion at an appropriate location, atrio-pathic arrhythmias were infrequent.

These observations are consistent with the hypothesis that preexisting occult atrial disease with concomitant systemic embolization is a frequent cause of non-hemorrhagic stroke.

An alternative explanation of the association between atrial dysfunction and non-hemorrhagic stroke is that various types of brain injury or stimulation may cause cardiac arrhythmia, other ECG-changes and even myocardial damage. An excellent review of this subject was given by Weidler (25). Abildskov et al. (26) point out that stroke patients are easily falsely considered to have primary cardiac disease. However, in young patients with non-hemorrhagic stroke the routine ECG only infrequently shows atrio-pathic arrhythmia (27). In the present study the prevalence of atrio-pathic arrhythmia increased by age both

among patients and controls. Together these and our results are consistent with the conclusion that atrio-pathic arrhythmias in stroke patients represent an intrinsic age related atrial disorder rather than atrial dysfunction due to the current cerebral lesion. Norris et al. (22) observed sinus bradycardia during coning. None of our patients, however, was in the stage of coning during LTER and only two patients expired as a direct consequence of the cerebral damage, the remaining five having secondary causes. Lavy et al. (29) monitored stroke patients immediately following arrival at hospital and compared the arrhythmias detected by monitoring with prior routine ECGs when available. They arrived at the "impression" that most of the arrhythmias were caused by the stroke. However, their most important finding may be that no less than 11 of 43 patients with non-hemorrhagic stroke had documented preexisting arrhythmia. Goldstein (24) compared the ECG in stroke with prior recordings and found that AF was over-represented in stroke patients as compared with controls and that it was frequently observed prior to the stroke. The importance of preexisting arrhythmia was also demonstrated by Friedman et al. (29). They compared previous ECGs of stroke patients with those from age and sex matched controls with the same blood pressure. The major difference between stroke patients and controls then was arrhythmia and digitalis therapy.

The criteria used for the diagnosis of an episodic SSS may appear to be too permissive but several facts support them. The majority of our patients with the SSS had the BTS-type including AF/AT, i.e. more than one type of arrhythmic evidence of atrial disease. However, in the Malmö series of episodic SSS patients with purely bradycardic SSS still had a considerable risk of embolization. Furthermore, the risk for developing stroke was unrelated to the severity of the bradycardia (16). This view that even mild sinus bradycardia may be the sign of a serious condition is supported by the report of Hinkle et al. (30) which revealed that this arrhythmia is associated with an increased risk of death. In the Malmö series of episodic SSS 30 autopsies were performed: Nine patients had single and 5 had multiple encephalomalacias and 17 instances of non-cerebral arterial embolizations were found in 11 patients. A left atrial thrombus was found in 6 of the 30 patients. These post-mortem results from patients with episodic SSS are similar to those obtained from patients with atrial fibrillation (5-8). Thus, in both types of atrial arrhythmia systemic embolization is a common phenomenon. And since chronic AF may be the end stage of the SSS (31) it seems possible that some of the

patients with AF and embolization belong to the SSS-entity rather than being "atherosclerotic" or "idiopathic".

In conclusion, we find that 44% of the patients in this series of non-hemorrhagic stroke had atriopathic arrhythmia during LTER. Sufficient evidence was obtained to warrant the conclusion that atrial disease or dysfunction as reflected by atriopathic arrhythmia may have caused a substantial proportion of non-hemorrhagic stroke in the present series. It is suggested that the SSS and AF/AT are to be considered as a common group of atriopathic arrhythmias reflecting atrial disorder predisposing for left atrial thrombus formation and subsequent systemic embolization.

As recently suggested by Easton and Sherman (32), we find that the LTER has proven its value in providing etiological information and deserves wide-spread application for this purpose. If the concept of episodic atriopathic arrhythmia reflecting atrial disorder can be confirmed as a frequent cause of systemic embolization this should have implications for future efforts in the primary and secondary prevention of non-hemorrhagic stroke.

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